The New England
Journal of Medicine

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VOLUME 218 JANUARY 13, 1938 NUMBER 2

MASSACHUSETTS MEDICAL SOCIETY

Section of Radiology and Physiotherapy

Presiding:
Dr. William G. Curtis, Wollaston, chairman.
Dr. Frank E. Wheatley, Milton, secretary.

THE CHAIRMAN: Our first paper is by Dr. Francis P. McCarthy. His subject is "Physical Modalities in the Treatment of Discrete Superficial Skin Lesions."

PHYSICAL MODALITIES IN THE TREATMENT OF DISCRETE SUPERFICIAL SKIN LESIONS

FRANCIS P. MCCARTHY, M.D.*

BOSTON

THE use of physical therapeutic modalities in the eradication of superficial skin lesions, with particular reference to benign and malignant growths, has reached a stage where after several years we can more definitely evaluate their effects. Merely to consider the clinical phase of such lesions would be academic and unnecessary, but a knowledge of the histopathologic structure of a given lesion is essential to the intelligent use of physical therapy.

The treatment of many discrete skin lesions such as warts, various types of nevi and even malignant neoplasms is left to every sort of medical and lay practitioner, including the "beautician," the podiatrist, the electrolysis technician and even the barber. When one considers the difficulty of diagnosing many of these lesions, even for the dermatologist, trained to interpret such conditions both clinically and histologically, it seems necessary to present a few fundamental facts in order to discourage the indiscriminate use of physical remedies. In discussing the treatment of discrete superficial lesions in the skin and the oral cavity, I shall attempt to indicate the proper modality called for by the clinical and histologic factors in the given case.

In general, it is desirable to note the location, size, color, consistence, depth and morphology of the lesion. If it is fairly large, and the diagnosis cannot be definitely determined, a small biopsy specimen should be taken and examined histologically. If the lesions are multiple, excision and examination of a single lesion may be desirable. It is not an uncommon practice among the untrained to commence treatment without first determining the character of the growth.

As a pathologist I have been impressed by the frequent use of unnecessarily radical surgical procedures in the removal of simple benign lesions, such as the excision of a large V-shaped wedge of tissue from the lip or tongue for a simple retention mucous cyst. On the other hand, inadequate treatment of a rapidly growing squamous-cell carcinoma may favor metastases to the regional lymph nodes.

Among the physical agents used are the following:

- Radium
- Roentgen rays
- Grenz rays
- High-frequency current:
  - Cutting current
  - Electrodesiccation
  - Electrocoagulation
- Electrocautery
- Actual cautery
- Electrolysis (galvanic current)
- Carbon-dioxide snow
- Ultraviolet rays

High-frequency current and carbon-dioxide snow I have found especially advantageous in the removal of benign and malignant superficial lesions. The use of radium and roentgen rays has been limited to deeper and more extensive lesions, which are not covered in this discussion.

The following tabulation indicates the wide variety of skin lesions which it is essential to recognize in order to apply the proper treatment:[1, 2]

Presented at the annual meeting of the Massachusetts Medical Society, Boston, June 1, 1937.

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- Verrucae (many different types)
- Keratoses
  - Senile
  - Leukoplakia
  - Kraurosis vulvae
  - Miscellaneous
- Nevi
  - Vascular
  - Solid cellular
- Keloids
- Tuberculides
- Cicatrices
- Multiple benign cystic epitheliomas
- Dermatitis papillaris capillitii (acne keloid)
- Chondrodermatitis nodularis chronica helicis
- Clavus
- Fibroma
- Granuloma pyogenicum
- Xanthoma
- Xanthelasma palpebrarum
- Adenoma sebaceum
- Retention cysts (mucous)
- Sebaceous cysts
- Telangiectases
- Molluscum contagiosum
- Basal-cell epithelioma
- Squamous-cell epithelioma
- Melanocarcinoma

There are many other skin lesions in which physical therapeutic measures may be applied.

I have selected from the list of cutaneous lesions several for discussion.

VERRUCAE

Verruca Vulgaris. The common wart occurs at all ages, but more often in the young, and tends to be autoinoculable. The histologic picture presents an entirely epithelial reaction — acanthosis and hyperkeratosis. In older people this lesion is often quite resistant to treatment, and carbon-dioxide snow with electrodesiccation offers the best form of therapy. In young children carbon-dioxide snow is the most desirable method of treatment; pressure is exerted for about twenty seconds, and the procedure is repeated two or three times, depending on the size and consistence of the lesion. Overtreatment is to be avoided, as it causes unnecessary scars.

Verruca Plantaris. The plantar wart has become more frequent in recent years than formerly, especially in women, through the wearing of thin-soled shoes; it presents a difficult problem in therapy, especially if only palliative measures are adopted. While x-rays and radium are both extremely useful here, I prefer the electrodesiccating current, with novocain injected deeply under the keratotic central plug of tissue, and with the fractional method of treatment. In some cases a complete removal may be effected at one sitting, but discomfort may be experienced during the healing stage.

Verruca Acuminata. This type of new growth may be small or may represent large conglomerate condylomatous lesions. Curettage under local anesthesia before use of high-frequency current is sometimes desirable. Venereal warts are most successfully treated by electrodesiccation, although both carbon-dioxide snow and electrolysis give good results.

Miscellaneous. Warts occur not infrequently on the eyelids; they are usually filiform, and a very slight desiccating current is normally sufficient to eradicate them without scars. Where the scalp is the site of the lesion, care should be exercised not to overtreat, as there is some danger of localized permanent alopecia, although this is a rare occurrence. Recurrences in the scalp are very frequent, and small lesions are readily overlooked. Probably the most obstinate type of wart is that on the bearded portion of the face. It is generally small and flat, or filiform. High-frequency current skillfully applied is usually effective, but scarring is the rule rather than the exception, and recurrences are common as a result of reinoculation from shaving.

KERATOSES

Keratotic lesions may be either primary or secondary, and include precancerous lesions. Clinical experience is essential for their recognition. The seborrheic type is quite common; it usually begins in middle life and involves the face and trunk. The lesions are brownish or almost black, greasy, soft and multiple. There is a marked hyperkeratosis of closely packed horny lamellae, and moderate to marked irregular acanthosis, with a distinct basal layer. There is a nevoid grouping of the epithelial cells, with horn cysts in the epidermis and inflammatory reactions of varying degrees in the upper corium. The lesions are readily removed by carbon-dioxide snow or light electrodesiccation, and no scarring should result. They do not tend toward malignancy, but occasionally give rise to the basal-cell type of lesion.

Keratosis Senilis. This is one of the commoner types and occurs principally on the face and the backs of the hands in individuals beyond middle life. The lesion may be indistinguishable from the seborrheic type, but is usually harder and more deeply pigmented. It is serious in nature, as it tends toward malignancy of the squamous-cell type, and often shows an invading ulcerative process beneath the overlying hyperkeratotic and acanthotic epithelial one. Radical destruction is indicated, although a biopsy may be advisable in order to ascertain whether a carcinoma has developed. It is interesting to note that while a squamous-cell epithelioma arising from a lesion on the face above the mouth tends to be locally malignant, those on the lip or neck metastasize to the cervical lymph nodes, especially if they are growing rapidly.

Electrodesiccation in the keratotic stage is in most

cases sufficient, but if the lesion is ulcerated and shows definite induration and ulceration, or if malignancy is present, excision with the cutting current or surgical excision may be necessary. In the treatment of senile keratoses, the resultant scar should not be taken into consideration, for the lesions are often malignant and thorough treatment is indicated.

Figure 1. *Leukoplakia buccalis (Grade 4) — verrucous squamous-cell carcinoma.*

Leukoplakia.[3] This common hyperkeratotic, acanthotic oral lesion, is graded in four groups, according to its clinical appearance and histopathology.

Grade I is characterized by the initial reaction of the mucous membrane to irritation, indicated by a red, granular, sharply defined and slightly sensitive area which soon becomes whitish gray. The microscopic picture at this stage shows an inflammatory reaction of the corium without definite epithelial proliferation.

Grade II is a very distinct lesion characterized by bluish-white patches or plaques without palpable induration, but sharply outlined from the normal mucosa. They are quadrangular or irregularly polygonal, and seem to be applied to the mucous membrane.

Grade III is very definite and is easily recognized at a glance, even by a laymân. It presents a milk-white, pearly or silvery indurated plaque, either localized or covering large areas. The lesion tends to wrinkle, especially if it involves the buccal mucosa. Microscopically the classic picture of marked hyperkeratosis, with acanthosis and cellular reaction of the corium, is seen.

Grade IV is a still more pronounced keratotic lesion, which is indurated and leathery in appearance and displays evidences of malignancy — early erosion, fissuring of the plaque or warty proliferation of the surface. This grade of leukoplakia should be treated as an incipient malignant neoplasm.

In the lesions of leukoplakia, the most striking histologic change occurs in the epithelial layer, especially the horny layer, which is markedly hypertrophied; in many cases the flattened, nucleated, hyperkeratotic epithelium extends clear up to the surface of the specimen. The rete cones are enlarged and broadened, and the malpighian layer is distinctly thickened. In the more advanced stages the hypertrophy of all the epithelial layers, especially the horny layer, is noticeable. Edema of the acanthotic cells may occur; in the early malignant stage the orderly arrangement of the malpighian layer is disturbed, with the formation of atypical cells, and numerous mitoses may be found.

Figure 2. *Leukoplakia buccalis (Grade 4). Shows marked hyperkeratosis and acanthosis with increased vascularity and cellular infiltration of tunica propria.*

Underlying the corium is usually a fairly pronounced cellular infiltration, with separation of the collagen fibers and diminution of the elastic fibers.

Except for the preventive measures of removal of the irritating factor in the mouth, together with abstinence from tobacco, the treatment of leukoplakia is unsatisfactory. Where tobacco is a factor and the patient continues to use it, removal is usually followed by a recurrence. Having tried various methods, I have virtually abandoned radium and x-ray in favor of electrodesiccation and electrocoagulation by monopolar and bipolar high-

frequency current. I have not employed the actual cautery, but believe it to be equally effective. I feel that the use of radium for leukoplakia of the tongue associated with atrophic luetic glossitis is provocative of malignancy where the treatment has been given in small doses over a considerable period of time. Malignancy has developed in 2 of my cases following this type of treatment where the radium plaque in 5- or 10-mg. doses was used for from twenty minutes to half an hour. Treatments over a period of months ultimately resulted in the development of verrucous carcinomatous lesions. It is advisable in this type of case to stop all smoking, to keep the patient under close supervision and to use monopolar or bipolar electrocoagulation in the destruction of any lesion that tends toward malignancy. Since it is in such cases that multiple malignancies of the tongue develop, great care should be exercised in their examination, and the patient should report every few months. The vast majority of leukoplakias require no treatment and the use of local irritating or caustic remedies is contraindicated, as there is a possibility of stimulating a malignant change.

Kraurosis Vulvae. This lesion represents a type of hyperkeratotic lesion that tends toward malignancy more frequently than does leukoplakia buccalis. Destructive desiccation or bipolar coagulation is recommended, or surgical excision in pronounced cases.

Miscellaneous. In the miscellaneous group of skin keratoses are those that follow the use of arsenic and are found on the soles and palms. They tend to develop into the squamous-cell type of malignancy, and are best removed by electrodesiccation. Keratoses following x-ray or radium burns often give rise to malignancy and are difficult to treat; due to the underlying fibrosis and avascular tissue, they are apt to ulcerate if destroyed.

NEVI

Birthmarks are quite common and of many varieties, and their differentiation requires considerable diagnostic skill. In describing their treatment it is desirable to point out the various types, with particular reference to the tendency of some of them to become malignant, and to emphasize the necessity of discretion and judgment. More than thirty types have been described, but for the sake of simplicity these may be divided into two broad groups, the vascular and the solid cellular.

Vascular Nevi. These are common, particularly in infants and young children, and consist of four varieties — nevus araneus (spider nevus), nevus flammeus (port-wine mark), and two kinds of angioma, the so-called strawberry hemangioma and the cavernous hemangioma.

Nevus araneus is a very superficial hemangioma, showing dilated capillary vessels emanating from a dot-like center. Either the galvanic needle or the high-frequency current may be used, the central spot being touched very lightly with the point of the needle; as a result, the lesion shrivels without leaving a scar.

Port-wine birthmarks are best left alone, especially if they cover extensive areas. Carbon-dioxide snow may blanch them out to a certain degree, but it is very difficult to achieve a uniform blanching, and the mottled effect may in the end present a more objectionable cosmetic effect than the original lesion.

Figure 3. *Cavernous hemangioma of tongue.*

Cavernous hemangiomas are composed of relatively large vessels lined with endothelium; they occur deep in the skin and subcutaneous tissue, and are best treated with radium or x-ray therapy, depending on their size. Carbon-dioxide snow is recommended for small, superficial lesions. With pressure applied for about twenty seconds for three or four times, the lesion gradually shrinks and disappears, leaving a thin, smooth scar. Electrodesiccation and coagulation have also been employed in the treatment of small lesions, but I have found the former method preferable; freezing produces a thrombosis of the vessels, associated with an acute inflammatory reaction and necrosis. Very satisfactory results are obtained with intervals of from two to four weeks between treatments.

In superficial vascular nevi of the strawberry

type, pressure treatment, with the water-cooled ultraviolet lamp to produce vesiculation, is very effective, and is comparable in its results to carbon-dioxide snow.

Solid Nevi or Moles. Pigmented nevi may be simple, brownish-pigmented lesions, definitely benign in structure and course, or deep black to bluish and dangerous in their potential tendency to malignancy. It is in this class of skin lesions that a

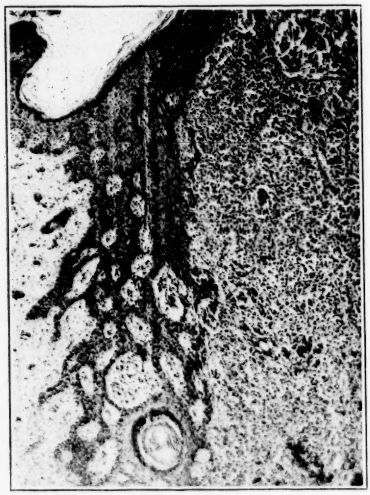

Figure 4. *Melanocarcinoma arising from pigmented mole of arm (fatal case).*

knowledge of the clinical and histopathological structure is essential in evaluating the proper physical modality.

The common mole is small, oval, smooth, slightly elevated and pale brownish, with or without the growth of hair; it cannot be considered potentially malignant in view of the many millions of seed moles in existence. However, even the most benign mole, if subject to traumatism over a period of years, may take on active growth tendencies and become a malignant neoplasm, with an early tendency to blood-stream metastases.

Blue-black moles are best left alone or removed by wide excision, as the underlying nevus cells may extend a considerable distance from the periphery of the lesion. If situated where chronic irritation may stimulate growth they are especially dangerous, as they frequently take on malignant tendencies with the production of one of the most rapidly growing neoplasms — melanocarcinoma.

MISCELLANEOUS

Keloids:[4] Keloidal growths of tissue represent hypertrophy of the collagen fibers of the corium, and may be spontaneous, or may follow scars from previous trauma or surgical incision. They occur in naturally susceptible individuals, and may even follow simple therapeutic procedures such as the removal of verrucae by electrodesiccation. Negroes and dark-skinned Caucasians have a special tendency toward these lesions. Surgery and electrosurgical therapy are contraindicated; radium for small lesions and roentgen therapy for larger ones give the best results.

Tuberculides. Many of the smaller, more superficial tuberculides may be treated by electrodesiccation with good results, especially if the lesions are discrete and cover extensive areas. The sarcoid

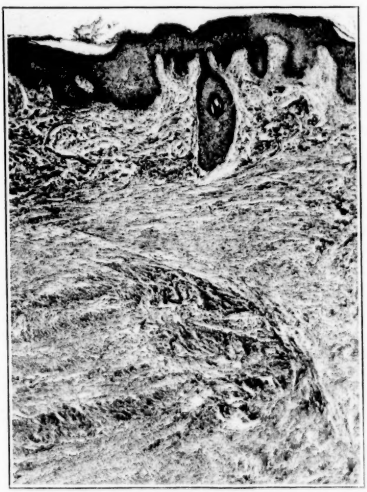

Figure 5. *Keloid showing interlacing collagen fibers.*

of Boeck, verrucous lesions and focal areas, and discoid lupus erythematosus lesions are amenable to the desiccating current. Carbon-dioxide snow also may be utilized in the treatment of lupus vulgaris nodules and in lupus erythematosus. One must not, however, fail to realize that internal medication with the arsenicals, gold compounds and bismuth is applied with beneficial results in cutaneous tuberculosis, and that physical modalities are merely adjuncts in the therapy of these lesions.

Dermatitis Papillaris Capillitii (Acne Keloid). This lesion, usually located at the nape of the neck,

may present a hard problem in therapy. I have found electrodesiccation, followed by radium or roentgen therapy, effective.

Granuloma Pyogenicum. This lesion is made up of granulation tissue, richly vascular and very persistent. Electrodesiccation, followed by curettage and further desiccation, generally destroys the

Figure 6. *Basal-cell epithelioma of upper lip.*

lesion, but unless the treatment is thorough a rapid recurrence is the rule.

Xanthoma and Xanthelasma Palpebrarum. The smaller lesions of xanthoma tuberosum may be destroyed by electrodesiccation, and excellent results are also obtained by it in xanthelasma of the eyelids. With the latter it is desirable to use a very small spark, as the cells comprising the lesion are highly susceptible to the electrical current, and promptly melt away upon a very light application. It is better to use fractional treatments than a single treatment that may be too severe, as disfiguring scars may be produced.

Retention Cysts. Mucous retention cysts of the lips and oral cavity are best treated by electrodesiccation. An initial incision with expression of the contents may be desirable in the larger cyst, followed by the insertion of the electrode and the application of sufficient current to destroy the epithelial lining. Small sebaceous cysts of the skin may be treated along similar lines, but the ideal treatment of the larger cysts is surgical resection.

Telangiectases. The enlarged superficial veins in old scars secondary to radiodermatitis may be destroyed by electrodesiccation, but as these ves-

Figure 7. *Cystic basal-cell epithelioma (eyelid).*

sels are compensating for the poor circulation in the cicatrix, ulceration may follow if the treatment is too drastic.

Figure 8. *Squamous-cell epithelioma of cheek (Grade 1).*

Molluscum Contagiosum. These lesions represent invaginated dyskeratotic epithelium and are readily shelled out by the curette; desiccation may be applied to the base of the lesion.

Basal-Cell Epithelioma. The basal-cell tumor is the common malignant lesion of the face; it has a characteristic appearance and can usually be diagnosed clinically without a biopsy. It is locally malignant and does not metastasize to the regional lymph nodes, but a certain percentage of these tumors contain epithelium of the prickle-cell type, in which cases more radical treatment should be applied. I have found electrodesiccation or coagulation the ideal treatment for a large number of these cases, in place of radium and roentgen-ray therapy. Often a combination of radiation and electrodesiccation is desirable, and the resulting scar is usually superficial and soft.

Squamous-Cell Epithelioma.[5] The method of choice in the treatment of this type of malignancy is based on each individual case, with special reference to the grade of malignancy, the size and location of the lesion, and the question of metastasis. In early and superficial lesions electrodesiccation or coagulation may be sufficient to destroy the lesion, but more often a combination of electrosurgery and radiation therapy is required.

SUMMARY

The clinical diagnosis of superficial lesions of the skin and the oral cavity is essential to an intelligent application of the proper physical modality. A knowledge of the histopathology is desirable so as to enable one to "read" the lesion in terms of the actual cellular process. Too often inadequate or too radical procedures are applied in treatment, based on ignorance of the clinical and histologic picture, and occasionally a metastatic, neoplastic process is caused by crude therapeutic methods.

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Discussion

THE CHAIRMAN: The discussion will be opened by Dr. Austin W. Cheever.

DR. AUSTIN W. CHEEVER, Boston: Dr. McCarthy does not leave me very much to say, for he has covered the subject very well indeed; however, there are one or two points that come to my mind. One is that I wish there were more control of beauticians. A little while ago, what I supposed was a mole on an eyelid turned out to be melanotic carcinoma. I wonder what would have happened if a beautician had been removing the "blemish." With only a galvanic needle, and no radium or diathermy, he might have done irreparable harm.

I think each one has his favorite methods. Some of mine differ from Dr. McCarthy's; for instance, I prefer radium on keratoses and epitheliomas. On plantar warts I like the x-ray best of all. It does not always work, but it seems to have a good effect in about 80 per cent of all cases. It is not the slightest bit uncomfortable to the patient. If it does not work, then there are other things to be done.

I suspect that all the warts are related. Can you tell me whether that is so? Is the seborrheic wart in the same class as the others?

DR. MCCARTHY: Pathologically it is.

DR. CHEEVER: It seems so clinically. We see the seborrheic type on back and face, the little pedunculated ones on the neck and in the axillae, and little flat abortive ones on the backs of the hands, all on the same patient.

I should like to stress the advantage of treating all the warts on the same individual and on other members of the family at the same time. In one family of eight, all have warts. I can persuade three or four of them to come in within a week or so of each other for treatment, but the rest will not do so. As a result I have seen each member of this family probably four or five times unnecessarily.

In nevus flammeus I did not hear Dr. McCarthy suggest ultraviolet rays; I think they are of some value. I agree with him that carbon-dioxide snow is likely to cause a very unpleasantly mottled scar, and x-ray and radium result, I believe, in one almost as bad.

The so-called strawberry mark should usually be treated less cruelly than is usually done. One doctor has said that radium is the best treatment but that it should be aimed at the wall and not at the skin, because such lesions almost always disappear spontaneously. During the World War I examined the skins of from 75,000 to 100,000 recruits. I did not see one strawberry mark among them; yet in any of our children's hospital outpatient departments we see a number of these marks, indicative that most of them disappear spontaneously. Outside of this, I certainly agree with Dr. McCarthy.

I want to emphasize his statement that one should understand the pathology of these lesions before tampering with them, not necessarily the pathology of the identical lesion concerned, but certainly the pathology of that particular type of lesion.

THE CHAIRMAN: It is now necessary to appoint a committee to nominate officers for next year. It is customary for the chair to name this committee, and I nominate Dr. Franklin P. Lowry and Dr. Herman A. Osgood.

Three years ago Dr. William Bierman came to us and gave us the result of his research work. He now has two more years of splendid work to his credit. He will talk to us on "The Treatment of Gonorrhea in Women by Means of Systemic and Additional Pelvic Heating."

THE TREATMENT OF GONORRHEA IN WOMEN BY MEANS OF SYSTEMIC AND ADDITIONAL PELVIC HEATING

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THE object of the technic which we employ to treat gonorrhea in women is the destruction of the gonococcus within its human host by thermal means. That this can be accomplished at temperatures which the human organism can withstand is amply proved by in vitro experiments, as well as by the clinical experience of other workers and of ourselves. Our technic differs from that described by others in that we apply higher temperatures (108 to 110°F., or 42.3 to 43.5° C.) to the female pelvis while the systemic temperature is simultaneously held at a lower level (at about 106°F., or 41.2°C.) This permits more effective heating in the region where the organism exists — when its ravages are localized to the organs within the pelvis.

To produce this systemic and differentially increased pelvic heating, we first elevate the temperature of the entire body. For this we have employed the short-wave currents alone, a horizontal photothermal cabinet placed over the patient as she lies in bed, and the hot-water bath. At present we use a combination of photothermal and short-wave heating.

Our cabinet contains twelve 60-watt carbon filament lamps arranged so that two, four or twelve may be switched on or off at one time. By means of overhead pulleys and a counterbalancing weight this cabinet is easily lowered or raised over the patient, as she lies on a mattress placed on a wooden table. The entire body except the head is covered by the cabinet.

The patient — who has been previously examined so as to determine that she is not suffering from any disease (aside from her infection) which would contraindicate the treatment — has been given an enema and a light breakfast by way of preparation. Her feet have been wrapped in cotton and her legs encased in cotton leggings to prevent the possibility of a burn. Except for these leggings and a bed sheet placed over her, the patient lies nude within the cabinet.

To speed the elevation of systemic temperature, the conversive heating energy of the short-wave current is utilized. Two condenser pads 30 by 40 cm. each are placed under the table so that one lies parallel to the region of the upper back and the other parallel to the area of the mid-thighs. These pads are connected to a short-wave machine of the type usually employed for routine treatment purposes, which produces a current of 50,000 megacycles (6-meter wave length).

Within about two hours the systemic temperature becomes elevated to approximately 106°F. (41.2°C.) The auxiliary energy of the short-wave current is then dispensed with and the apparatus for additional pelvic heating is applied. If the patient has shown evidence of acute peritoneal inflammation, as indicated by the presence of fever, lower abdominal pain and tenderness, the application of local pelvic heating is deferred for three or four hours.

We have found that the most effective method of applying local heating is by means of diathermy. Short-wave energy administered by metal vaginal electrodes can be used for this purpose. Our first experience in the simultaneous systemic and higher pelvic heating was gained by the use of these currents.[1] However, it is our impression that it is possible to localize the heating effect produced by diathermy more accurately than we can by means of short-wave currents. With the latter the heating process must continue for a period of from six to eight hours, and when this has been done, we have observed occasional overheating of the structures on the inner sides of the thighs. To avoid such local overheating with its painful sequelae, we apply the dispersive diathermy electrodes as follows. A metal belt about 8 cm. in width and made of flexible lead-tin composition metal (such as is ordinarily employed for the administration of diathermy treatments) is placed around the waist. Two similar metal cuffs are placed around each thigh. These three electrodes are connected to one terminal of a diathermy machine. The other terminal is connected directly to the vaginal electrode. To arrange for still further dispersion of the current we take a large metal electrode about 25 by 30 cm. in size and place it on the back of the patient, so that it makes definite contact with the posterior portion of the metal belt placed around the waist. In the circuit of each of the electric cables going to the three dispersive electrodes we have a milliampere meter and a variable resistance. The purpose of this arrangement is to indicate the

Presented at the annual meeting of the Massachusetts Medical Society, Boston, June 1, 1937.

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amount of current energy flowing along each cable. If we find that there is an undue amount of current flowing to one thigh, for example, we increase the resistance in that portion of the circuit, so that the current energy going to the other thigh becomes equalized. After about three hours the thigh cuffs are shifted to the calves.

The vaginal electrode which we use is patterned after plaster casts which we have made of numerous adult vaginas. The metal electrodes which have been made from these plaster casts come in four sizes, varying from 7 to 11 cm. in length. The metallic mass of the electrodes and the handles connected to them are channeled so as to permit the insertion of a thermometer.

The thermometer serves as our guide in determining the quantity of diathermy current which is to be applied. It is specially constructed so that, through prisms on either side, its mercury column is readily visible for a distance of several feet. This makes it possible to read the thermometer through the window of the cabinet. The markings on the thermometer are widely separated, with gradations indicating 0.2°F. That amount of diathermy current is permitted to flow which will heat the tissues to a temperature which, transmitted through the metal of the electrode to the thermometer, registers between 109 and 110°F. (42.8 and 43.5°C.).

The pelvic temperature is held elevated at this higher level while the systemic temperature is maintained at about 106°F. (41.2°C.) The determination of systemic temperature is made by means of thermometers inserted into the mouth and the axilla. Before starting pelvic heating we determine the relation between the temperatures in the mouth, axilla and rectum. This helps to indicate the systemic temperature as judged by the elevation in the rectum. When the rectal temperature is no longer available as a guide, owing to the distortion produced by the pelvic heating, the mouth temperature is used and is generally considered to be about 0.7°F. below the rectal temperature.

The systemic temperature elevation is maintained for about twelve hours. During this time the patient receives fluids, either plain cold water or cold 0.6 per cent saline solution, in quantities as large as she desires. To minimize her discomfort she is given sedation, usually 1/200 gr. of hyoscine hydrobromide in combination with 1/6 gr. of morphine sulfate. If necessary, small doses of morphine are repeated.

In addition to observations of temperature, the general condition of the patient is noted continuously, as determined by the color of the face, rate and character of the pulse, and so forth. Close and continuous watchfulness is essential in order to avoid untoward effects.

The purpose of the higher temperatures in the pelvis is to achieve the quicker lethal influence on the gonococcus. At 106.7°F. (41.5°C.) Carpenter and his co-workers[2] have shown that the various strains of the gonococcus will resist heating for periods varying from six to thirty hours. At 109.3°F. (42.8°C.) the killing time is cut to about one half. We recognize that in addition to the direct thermal injury there are immune factors which serve to produce the death of the diplococcus within its human host. It is our experience that this treatment may be applied at any stage of gonococcal infection. However, we prefer not to administer the treatment in the period two days prior to, during and two days after menstruation. If pregnancy be present, there exists the possibility of doing damage to the fetus because of the high pelvic temperature.

We have had the opportunity of treating 125 women by means of this technic. In all these the diagnosis was confirmed by the direct observations of the organism in the cervical or urethral secretion or in both. One hundred and seventeen of these (93 per cent) were freed of gonococci. In our first series, consisting of 67 women who received from five to six hours of general hyperpyrexia, during three and a half to four hours of which additional pelvic heating was administered, 62 were rendered gonococcus-free in an average of 2.3 treatments per patient. In our second series of 58 women who received twelve hours of hyperpyrexia, including from six to eight hours of additional pelvic heating, in 55 the gonococcus disappeared after an average of 1.4 treatments per patient.

The determination of the necessity for re-treatment is based upon the finding of the organisms in cervical or urethral discharges on the day following the treatment. If the stained smears are negative, further examinations are continued at daily intervals for several days. The necessity for re-treatment depends on thermal resistance of the organism responsible for the infection and upon the immunity of the patient.

Within a few days following adequate treatment, there is a subsidence or disappearance of the vaginal discharge. The cervical secretion becomes mucoid and clear, microscopically containing only scattered leukocytes instead of the pus clumps previously found. The urethral smear contains only scattered leukocytes in addition to many epithelial cells and Döderlein bacilli. In a few cases, superficial mucosal burns have caused a prolongation of the discharge; with the healing of the mucosal area within two or three weeks, the discharge disappears. In a few other cases, trichomonas vaginitis has caused a continuation of the discharge fol-

lowing the disappearance of gonococci. This discharge ceases with the application of measures directed against the vaginitis.

About one third of the cases were complicated by salpingitis. In the acute or subacute salpingitis cases, pain usually disappears after the first treatment. We have observed that treatments may be instituted at any stage of gonococcal infection, even in the presence of acute salpingitis, associated with fever and pelvic peritonitis. Tubo-ovarian inflammatory masses, including those which are probably suppurative and associated with a rapid sedimentation time, respond satisfactorily to this type of treatment. There is first a diminution or disappearance of pain, and a return of the temperature to normal the day following the treatment. The temperature remains normal. Rapid sedimentation rates become slower.

Pelvic examination within a few days after treatment usually reveals a marked lessening of pelvic tenderness, but little change in the size of the adnexal masses. From seven to ten days after treatment there is usually an increased mobility of the uterus and some shrinkage of the inflammatory masses. After about two weeks following the treatment, the adnexal masses become much smaller.

The first menstrual period following treatment sometimes comes on before the expected time, and may be more profuse and of longer duration than usual. We have never observed a cessation of menstruation or the occurrence of menopause symptoms after treatment. A number of patients with chronic salpingitis associated with painful or prolonged menstruation noticed that menstruation became more normal and less painful following treatment.

Pregnancies and normal delivery have occurred in a number of patients whom we have previously treated for gonorrhea by this technic. In a number of patients with acute salpingitis at the time of treatment, insufflation by the Rubin method has subsequently demonstrated normal tubal patency.

The follow-up on most of these cases has been sufficiently prolonged (in some cases extending for a period of five years) to assure us that the disappearance of the gonococci has been permanent. We have relied upon frequently repeated smears, especially those taken directly after the cessation of menstrual flow. In addition, in many cases we have made cultures. The danger of a woman's becoming reinfected by resumption of relations with the sex partner who originally infected her or with some other infected individual is always to be reckoned with. In 4 cases, after intervals of many months, during which repeated examinations failed to reveal the presence of abnormal discharge or of gonococci, a purulent discharge containing the organisms was again found. In each of these cases there was a definite history of new exposure to an infected partner.

SUMMARY

We have described the technic for the simultaneous production of systemic with still higher pelvic heating. Temperatures of 106°F. (41.2°C.) are achieved systemically, and of 109 to 110°F. (42.8 to 43.5°C.) within the region of the pelvis. This combined heating is maintained for a period of from six to eight hours. The interval of systemically elevated temperature is continued for a total of about twelve hours.

With this technic, as utilized in our last series of 58 cases, an average of but 1.4 treatments was found necessary to achieve the eradication of the gonococcus from its human host. With the disappearance of the organisms, associated symptoms disappear. Pelvic masses gradually subside. In our total series of 125 cases permanent disappearance of the organism was achieved in 117, or 93 per cent.

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2. Warren, S. L.; Boak, R. A., and Carpenter, C. M.: A correlation between the in vitro thermal death time of the gonococcus and the febrile period required at 41.5°C. for cure. New York: Fourth Annual Fever Conference, April 27, 1934.

THE CHAIRMAN: Will the nominating committee please report?

DR. FRANKLIN P. LOWRY: The committee nominates Dr. Frank E. Wheatley, of Boston, as chairman, and Dr. Herman A. Osgood, of Boston, as secretary.

Dr. Wheatley and Dr. Osgood were declared elected.

THE CHAIRMAN: I declare the meeting adjourned.

TRAUMATIC INJURY OF THE CONDYLOID PROCESS OF THE MANDIBLE

KURT H. THOMA, D.M.D.*

BOSTON

TRAUMATIC injury of the condyloid process is not easily diagnosed, and is often difficult to treat. It may occur in conjunction with a more obvious fracture of the body of the mandible, when it is frequently overlooked. Fortunately, fractures of the condyle often heal without special attention, particularly when prompt treatment by means of intermaxillary ligation and fixation of the jaw is given. There are exceptions, however. Untreated fractures complicated by dislocation may have permanent limitation of motion, and resultant discomfort during mastication. In edentulous jaws considerable shortening of the ramus and asymmetry of the face due to overriding of the fragments is liable to occur if correctly constructed splints are not used. In compound injury with fracture of the articular fossa, or in the presence of infection, ankylosis may result.

Traumatic injury to the condyloid process may be classified as follows:

I. Subluxation (unilateral or bilateral).
II. Dislocation without fracture (unilateral or bilateral).
  a. Forward.
  b. Backward.
  c. Upward.
III. Collum fracture (unilateral or bilateral).
  1. Overriding of fragments.
  2. Displacement of condyloid process.
    a. Forward.
    b. Medial.
    c. Lateral.
  3. Dislocation of the condyloid process.
    a. Medial.
    b. Lateral.
IV. Traumatic ankylosis (unilateral or bilateral).

SUBLUXATION

Subluxation is often the result of minor trauma such as occurs when difficult tooth extractions are attempted, with application of undue force by means of forceps or exolevers instead of the resection of a sufficient amount of alveolar bone to facilitate the operation. Careless use of the mouth gag during general anesthesia is another cause, producing rupture of the joint ligaments or injury to the meniscus.

The patient complains of weakness of the joint, felt when yawning or when undergoing prolonged operations in the dental chair. In some cases the condyle catches every time the jaw is opened wide, receding with a jumping motion. This is frequently due to the rupture of the attachment of the external pterygoid muscle to the meniscus, which causes the latter to remain in place during the forward movement of the mandible instead of being pulled forward. The condyle therefore slides off its anterior margin, producing a sound when it strikes the articular eminence; this sound often becomes extremely annoying to the patient, as it occurs principally while eating and is audible to others. Subluxation may be unilateral but is generally bilateral.

The motion of the jaw should be limited by a dental appliance, or motion should be entirely prevented by means of intermaxillary ligation, so as to allow the ligaments to regain normalcy. This may require from three to six weeks. Intermaxillary fixation is to be preferred to the use of a four-tail bandage — first because it is invisible, and secondly because the patient is unable to remove it. Liquid diet should be prescribed.

DISLOCATION WITHOUT FRACTURE

The mandibular joint possesses motion not possible in any other joint; therefore trauma will not always markedly increase its limitations, and dislocation may occur frequently without the joint capsule's being ruptured and without the condyle's piercing it. Dislocation is frequently associated with fracture at the neck of the condyle or the ramus, and indeed many dislocations can occur only in conjunction with fracture. These will be discussed later. Dislocation of the mandible without fracture occurs bilaterally more often than unilaterally.

Forward dislocation. Though comparatively rare, this type of dislocation is more frequent than others. It occurs occasionally in newborn infants during delivery, especially in head presentations, but is seen more often in adults. It may be caused by a blow on the chin when the mouth is open, by opening the jaws too far when yawning or by the injudicious use of a gag under general anesthesia. When dislocated the condyle rests anterior to the articular eminence, where it is locked by tension of the temporal, internal pterygoid and masseter muscles. The stylomandibular ligament, which is relaxed in ordinary forward motion, also becomes taut. The jaw remains in this position, as the combined effort of the muscles can no longer pull the head of the condyle back.

In acute forward dislocation the jaw is locked in

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a position that causes a so-called open bite. The chin is moved forward and down. Eating and talking is difficult, and there may be salivation and dribbling. In chronic dislocation the jaw slips back into its normal position more easily because the capsular and sphenostylomaxillary ligaments have been stretched. The patient, however, is well aware of the condition and fearful of repeated experiences, which are brought about from the slightest cause because of weakness in the articular attachments. Yawning or opening the mouth wide as during dental operations may bring on dislocation.

The symptoms, together with the prominence of the condyles, which can be easily palpated when the jaw is dislocated, aid in diagnosis. The latter may be verified by means of x-ray examination (Fig. 1).

In acute dislocation, reduction by means of any force that makes the muscles and ligaments yield is inadvisable. It would cause further injury of the tissues, analogous to that which is often the cause of chronic dislocation. Instead, careful manipulation should be resorted to, reversing the process of dislocation. This is accomplished by opening the jaw wide, depressing the chin, and forcing the lower end of the ramus upward and backward. The head is thus made to glide over the eminence and back into the articular fossa: the jaws can then be closed. The use of general anesthesia facilitates the operation through relaxation of the muscles.

In order to prevent recurrence in acute dislocation, the motion of the mandible should be limited for a few weeks by applying bands to the teeth, to which are attached intermaxillary elastics or a silk cord to limit the opening to 1 cm.

In chronic dislocation the prognosis is rather poor. If not of too long standing, rest as described for subluxation may be of help. When dislocation occurs frequently and is accompanied by complete locking, permanent appliances as described for the acute type may be constructed.

Case 1. The patient, a 42-year-old female, complained of protrusion of the jaw. The earlier history was irrelevant. The present complaint had started six weeks previously, when she had had her remaining upper and lower teeth extracted. The mandible protruded and could not be moved as before. There had been no accidents or injury.

Clinical examination revealed prominent condyles on both sides of the face. The motion of the jaw was limited. Roentgen examination of the mandibular joint showed the condyle anterior to the eminentia articularis on both sides. The diagnosis was forward dislocation of the mandible (Fig. 1).

Under ether anesthesia the condyles were manipulated to take their place in the mandibular fossae, when the true relation of the mandible to the maxilla was taken by placing wax plates previously prepared by the patient's dentist in the mouth and forcing the jaws into place. A temporary splint was improvised and held in place by a Barton bandage. Later the permanent splint constructed from the wax models was inserted and the jaw was held in

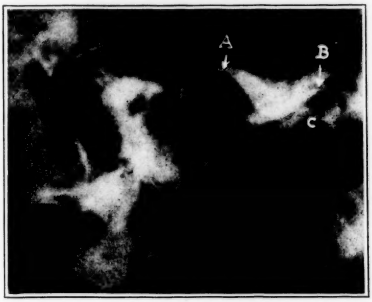

Figure 1. *Case 1. Forward dislocation of the mandible. The condyle is locked anteriorly to the articular eminence. A = fossa articularis, B = position of condyle (C), anterior to articular eminence.*

place by a four-tail bandage for 6 weeks. The result was satisfactory, and the patient had upper and lower dentures made and could wear them without trouble.

Backward dislocation. A blow directed backward against the chin may cause detachment at the posterior margin and forward displacement of the meniscus. The head of the condyle moves backward and upward, coming in contact with the glenoid fossa. This type of dislocation is fortunately of rare occurrence. I have seen it in the case of an automobile accident, the blow striking the chin without causing fracture of the body of the mandible. Hemorrhage which accumulates in the posterior part of the joint prevents the disk from returning to its normal position. In more serious trauma the bone may be crushed into the auditory canal; this may terminate in ankylosis (see below).

Such patients have the third molars in distal occlusion with open incisal bite (Fig 2). Motion of the jaw is interrupted when opening on account of interference from the displaced meniscus. In the case of fracture of the tympanic plate, bleeding from the ear is generally noticed and examination of the auditory canal may show obstruction.

Under ether anesthesia, with muscles well relaxed, the mandible is manipulated. Force is applied that tends to draw the condyle out of the articular fossa; this in turn may allow the meniscus to slide back into place. In order to keep the condyle out of the joint fossa until the tissue has recovered, the occlusal surface of the teeth should be raised in the upper jaw by inserting a rubber-plate

wedge made to fit over the posterior teeth. The jaw should not be immobilized, however, as motion is desirable to prevent fibrous ankylosis.

Case 2. The patient, a 30-year-old male, complained of inability to eat because he could not get his teeth to occlude, except the molars, and was unable to open his jaws wide on account of interference. He said that the surgeon who had treated him had asserted that under ether his jaw could be closed normally. The earlier history was irrelevant. The illness started after an automobile accident, when the maxilla was fractured on the right side; the fracture included the malar bone. The patient had since received treatment, and although the fracture had healed, his symptoms had not improved.

The clinical examination showed that the fractured part of the upper jaw had united too far lingually so that the teeth could not occlude normally. Furthermore, the incisors and premolars could not be brought into contact, as the last molar teeth on both sides came together and prevented closing of the bite. As this condition was the same on the left, where no fracture had occurred, it could not be attributed to the above-mentioned malunion. Sometimes the patient could open his jaw wide, but at other times something interfered and he could open it but little. X-ray examination was advised, and a provisional diagnosis of backward dislocation of the mandible with displacement of the interarticular cartilage was made.

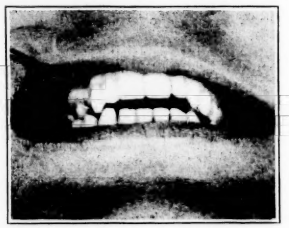

Figure 2. *Case 2. Backward dislocation. The condyle, being pushed back and up against the glenoid fossa, causes an open bite.*

The x-ray report was essentially negative. There was no evidence of fracture or malunited fracture in the region of the ramus or at the neck of the condyle.

With avertin and nitrous-oxide-oxygen anesthesia, osteotomy was performed on the right maxilla, and a previously constructed splint was applied so as to assure healing in a normal position. The defective occlusion of the mandible was not improved thereby. The anesthesia was supplemented with ether to get complete muscular relaxation so that the jaw could be manipulated. It was found that by forcing down the ramus the mandible could be occluded normally. After a few attempts the jaw remained in normal position when closed, presumably because the meniscus had moved back into its normal place. Intermaxillary ligation was then used; by wiring the teeth to the splint in the upper jaw it was hoped that the incisors could not be forced back into the opened position.

A Barton bandage was applied to prevent pulling down of the side where the maxilla was fractured. After 5 weeks the wires were removed, when it was found that the patient had no difficulty in closing his teeth normally, and that the opening motion was no longer interfered with.

Upward dislocation. This is extremely rare and may occur in conjunction with backward dislocation, or as a more serious condition when the condyle is forced through the glenoid fossa into the middle cerebral fossa. This is liable to happen where there are no posterior teeth to take up the force when a blow is directed to the anterior part of the mandible.

Reduction under general anesthesia should be followed by the application of a denture splint replacing the missing back teeth, the bite being opened at the same time. External drainage may be indicated. The splint should immobilize the jaw for four or five weeks. If ankylosis results, exercises with the purpose of forcefully opening the jaws are indicated. In extreme cases arthroplasty must finally be resorted to.

COLLUM FRACTURE OF CONDYLOID PROCESS

This is a common fracture, and probably occurs more frequently than statistics indicate, for in multiple fracture it is often overlooked. It is generally found at the lower part of the neck of the condyle (Fig. 3); it frequently involves part of the ramus, extending in an oblique direction downward to the posterior border of the bone (Fig. 4).

The fracture is caused by a blow on the chin, and is usually bilateral. It is often associated with fracture in the region of the symphysis. Unilateral fracture of the condyle may be associated with fracture of the mandible on the other side in the premolar or molar region. It may occur, however, as a single fracture when the blow is directed to the side of the face, for instance, in the region of the middle of the ramus. I have seen bilateral fractures caused by the following accidents: a girl of nine falling from a bicycle and striking her chin on the sidewalk, a rider falling when taking a hurdle, a flier landing his airplane, an amateur tree-chopper getting hit on the chin by the falling trunk, and several patients injured in automobile accidents. I have seen unilateral fractures in a boy who fell while roller skating, in a patient who received a lateral blow to the angle of the jaw, and in victims of automobile accidents. In one patient the collum fracture from a lateral blow was associated with fracture of the maxilla.

Collum Fracture with Overriding of Fragments

The overriding of the fragments is caused by muscular contraction. This is due to trismus resulting from collateral edema associated with the trauma. If most of the posterior teeth are present the condition is recognized by open bite in the incisor region. In jaws edentulous in the posterior part, it may be overlooked until after the swelling of the face has subsided, when we discover facial asymmetry, the angle of the jaw being higher and

the chin being moved toward the affected side. In cases where the jaw has united in such a position the patient complains of painful sensation in the joint and ear. This is due to pressure or friction caused by the condyle when moved in its abnormal relation.

Diagnosis is made by means of x-ray examinations of the joint from a lateral point of view and from an anteroposterior aspect. One or the other, or both, will show the deformity.

Treatment should be instituted as soon as possible after the accident. The fracture is reduced by means of manipulation under ether, followed by intermaxillary ligation if a full complement of teeth is present. In case of partially edentulous jaws a denture splint must be constructed before the reduction is attempted. This is inserted after satisfactory results have been obtained by manipulation, for the purpose of holding the jaws in proper relation while healing is taking place.

In malunion of long standing, discomfort in the joint may subside in time. If dentures are worn, these may have to be adjusted to the new maxillary relations, and this may also help to improve the condition. If pains are persistent, however, and radical surgical treatment is necessary, an osteotomy at the neck of the condyle may have to be performed, which when followed by fixation of the jaw in normal position will bring back normal relations. In complicated cases, osteoarthrotomy or arthroplasty may have to be resorted to.

Case 3. The patient, a 28-year-old female, complained of pain when moving the jaw, with pain in the ear and swelling of the face. The earlier history was irrelevant.

Figure 3. *Case 3. Collum fracture with overriding of fragment and shortening of the ramus due to muscular trismus. C = condyle, F = fracture line.*

The condition was caused by an automobile accident 2 days before.

On clinical examination the posterior maxillary teeth on the left side were freely movable with a large section of the alveolar bone. There was crepitus on the left side when the jaw was opened, and pain upon pressure applied in front of the tragus of the ear. Provisional diagnoses of fracture of the alveolar process of the maxilla and collum fracture of the left mandible were made. Roentgen examination was advised.

Intraoral films showed a fracture of the maxilla involving a fragment containing premolar and molar teeth. The mandible showed horizontal fracture through the neck of the condyle, with overriding of fragments and shortening of the ramus (Fig. 3).

Under ether anesthesia a splint was placed in the upper jaw to hold the fractured parts in position. The ether anesthesia deepened and when the muscles of the jaw became relaxed the fracture of the condyle could be reduced by manipulation. Fixation was secured by intermaxillary ligation. Recovery was uneventful, and the splints and wires were removed after 6 weeks. Normal motility was obtained after 10 days, during which the patient was advised to exercise the jaw systematically.

Case 4. This patient, a 24-year-old female, complained of a pain in the right mandibular joint and a crackling noise in the left one. She was unable to wear her dentures. She had been in an automobile accident 6 weeks previously, hitting the dashboard with the right side of the face (ramus). She had seen her family physician, who applied adhesive tape. Her teeth had all been extracted 7 months before, and she had had full dentures made 5 months before. These she had worn with comfort until the accident.

Clinical examination showed asymmetry of the face, the chin being drawn to the right; the median line of the lower denture was transposed about 1 cm. to the right, and the teeth therefore did not occlude. Movement of the jaw was not interfered with, but a noise could be heard when the jaw was opened. There was no crepitus or other indication of ununited fracture.

The roentgen examination consisted of lateral and vertical exposures. The latter revealed a malunited fracture at the neck of the condyle of the mandible on the right. There was a slight outward displacement of the condyle, and because of overriding the ramus was shortened. The outline of the mandible and its location were asymmetrical.

The patient was advised to have a new set of dentures constructed by her dentist. These proved successful. The pain in the joint was relieved, but the facial appearance was not greatly improved.

Collum Fracture with Displacement of Condyloid Process

Forward displacement. This is the commonest type of displacement, since the external pterygoid muscle is attached to the neck of the condyle at the pterygoid pit and in case of fracture draws the neck of the condyle forward. The condition is recognized in a lateral x-ray of the mandibular joint (Fig. 4).

Medial and lateral displacements. Lateral displacement is more common. It is caused when the ramus is pressed upward on the inside of the condylar fragment, locking it into position by contraction of the masseter and internal pterygoid muscles. Lateral x-rays show the overriding; the anteroposterior view, on the other hand, shows the medial or lateral displacement of the condyle.

Reduction is accomplished by manipulation

under avertin and ether anesthesia. The patient must be prepared for the operation so as to avoid postoperative vomiting. The jaws are immobilized for from five to six weeks by intermaxillary ligation or the use of splints. In cases of marked forward displacement, open reduction may be indicated. When the head of the condyle is moved into place it can generally be fixed by wiring the teeth, which is done by an assistant, the wound being protected by a piece of wet gauze. If this is not successful a galvanized nail may be placed anterior to the condylar fragment to hold the latter in place. It is allowed to project through the wound and is removed after a week or ten days.

Case 5. The patient, a 24-year-old male, complained of a fracture of the mandible, with bleeding from the chin, pain and inability to close the jaw. The previous history

Figure 4. *Case 5. Collum fracture, bilateral, with fracture at symphysis of mandible; the x-ray shows a fracture of the condyle on the left, with forward displacement of neck and overriding due to muscular contraction. C = condyle, F = fracture line.*

was irrelevant. The present illness started with an accident which occurred while the patient was cutting down a tree; the falling trunk struck him on the chin.

At the clinical examination there was pronounced swelling under the jaw and on the chin, where there was a contusion of the skin. There was a slight swelling of both cheeks. The mandible had been displaced and there was crepitus in the anterior part and the region of the joints. The left superior central incisor was loose, as well as the right inferior central.

In the roentgen examination anteroposterior and lateral exposures were made. These showed a vertical fracture in the anterior portion of the lower jaw, close to the median line. Here an unerupted tooth was seen, which lay horizontally. The tooth did not seem fractured, but the fracture line extended beyond it. The lateral view showed fractures at the necks of the condyles on the right and left sides. Both condyles appeared to be displaced anteriorly, and there was overriding due to muscular contraction (Fig. 4). Dental films of the upper teeth showed luxation of the left central incisor.

With premedication, pentobarbital sodium (3 gr. Nembutal), and gas-ether anesthesia, the retained tooth in the anterior part of the mandible was removed. The upper central tooth was extracted, as well as the lower one, which was found involved in the fracture. The jaw was placed in what appeared to be normal position and fixed with intermaxillary ligation. Roentgen examination after operation showed that manipulation of the fragments had not produced good results at the condyle. The patient was operated on again 2 days later. An external incision was made in front of the ear and extended at right angles along the zygomatic process. The condyles were exposed and forced into normal position. The patient was dismissed 11 days after operation. Healing was uneventful. Fifty-one days after the second operation the patient had normal union and could move his jaw well; occlusion was satisfactory.

Case 6. The patient, a 37-year-old male, complained of pain when moving the jaw and a swelling on the right side of the head. The previous history was irrelevant. The patient had a fall while taking a hurdle on horseback, injuring his left arm and shoulder, right ankle and face.

Clinical examination showed the region of the right condyle of the mandible to be tender on palpation; there

Figure 5. *Case 6. Collum fracture with lateral displacement. C = condyle.*

were pain and crepitus when moving the jaw. A provisional diagnosis of fracture of the ramus was made.

Roentgen examination of the left arm and shoulder, thoracic cage, right leg and foot, and skull showed no evidence of fracture. The anteroposterior view of the head showed a fracture at the neck of the condyle, displaced laterally. There was considerable overriding, due to muscular contraction (Fig. 5).

The fracture was reduced with ether anesthesia and the position retained by intermaxillary ligation. After 5 weeks the wires were removed and motion of the jaw was found to be normal except for slight muscular interference, which disappeared in a few days.

Collum Fracture with Dislocation of Condyloid Process.

Luxation fracture is not very common in the mandible, probably because of the free movement which is allowed the condyle in the joint. It oc-

curs as follows: the bone fractures but does not separate, and on account of continuance of the traumatic action the condyle is then pressed out of the capsule either medially or laterally. Compound dislocation is rare.

Medial dislocation. This is the common type of dislocation because of the action of the external pterygoid and the anatomic condition of the fossa articularis, which favors a medial dislocation rather than a lateral one. The meniscus generally remains in the fossa, while the condyle pierces the capsule. The cause may be a blow to the angle of the jaw, causing fracture at the neck without displacement, the continued force pressing the medially bent condyle out of the socket.

Case 7. The patient, a 9-year-old boy, had a swelling of the parotid region, and consulted his dentist on account of pain from an injured tooth. The dentist referred the patient for examination. The earlier history was irrelevant. Two weeks previously the boy fell on the sidewalk and injured a front tooth. The next day a swelling appeared in front of the ear on the left side, and he was put to bed, as he was thought to have the mumps.

Figure 6. *Case 7. Collum fracture with median dislocation. C = condyle, F = fracture.*

Clinical examination revealed a swelling in the zygomatic region; the patient could open his mouth only part way, and complained of pain when pressure was applied in the region of the condyle.

At roentgen examination the lateral view of the left side of the mandible showed an oblique fracture at the neck of the condyle without displacement. The anteroposterior view showed median dislocation of the head of the condyle (Fig. 6).

Avertin anesthesia supplemented by ether was used. An incision was made over the zygomatic arch, and the ramus was exposed. The condyle was located and pulled into place by means of a hook while the ramus was pressed down by an assistant. The condyle could then be seen functioning in the socket as the jaw was moved. The fascia was brought together and held by catgut sutures, and the incision was closed with horsehair sutures. The teeth were fixed in occlusion by intermaxillary ligation. When the wires were removed after 23 days the jaw was stiff, but when the patient was seen 5 days later he had regained normal function.

Lateral dislocation. This type is uncommon, as it is prevented by the very strong outer capsular ligament, and the protection afforded by the zygomatic arch. A case has been reported where the ramus fractured at the angle and the condyle was dislocated in a lateral and upward direction. In such cases compound fracture may occur.

The diagnosis is made by means of x-ray examination. The anteroposterior view best shows the dislocation (Fig. 6). The lateral view generally discloses the fracture line. There may be considerable swelling of the face. In the case reported above, this was mistaken for mumps and the patient received no treatment for two weeks.

Reduction is indicated even in cases of one or two weeks' standing, although the prognosis of an untreated dislocation is not bad, the condyle and ligaments having great power to adjust themselves to a new position, especially in children. If the fracture is incomplete, manipulation under general anesthesia may reduce the dislocation. As a rule, open reduction must be resorted to. The approach is through an incision along the lower border of the zygomatic arch, after which the condyle is located by blunt dissection. In lateral dislocation this presents no special difficulty; in median dislocation the external surface of the ramus should be exposed after detaching part of the masseter muscle. The condyle can then be located, taken hold of by means of an instrument with a half-round, pointed hook, and pulled back into position while the ramus is pressed down. The wound is then closed and the jaw fixed by means of intermaxillary ligation or a splint. In spite of fixation, the retention of the meniscus and of the synovial membrane, if intact, prevents ankylosis. In case of destruction of the joint, however, ankylosis may result, especially in children. In such cases an arthroplasty may have to be performed later. When using intermaxillary ligation for retention it is important that the patient have no posterior edentulous condition on the affected side, because undue pressure on the condyle may cause resorptive processes during the period of fixation.

After four weeks the ligatures are removed. Although the result may be good, the patient may not have normal function at once. Exercises must be prescribed to limber up the jaw and to increase motility.

TRAUMATIC ANKYLOSIS

Ankylosis of the jaw may follow traumatic injury, although it is more frequently caused by infectious arthritis, otitis media and osteomyelitis of the ramus. Orlow,[1] who wrote one of the most comprehensive articles on mandibular ankylosis, found trauma as the cause in 28 cases out of 100. In 23 of these cases the trauma was due to accidents such as a fall on the chin, a blow, or a fracture of the body of the jaw or base of the skull. In a few cases there was a compound fracture due to gunshot injury, and in 2 cases forceps delivery was the cause. We therefore find ankylosis resulting from a variety of traumatic injuries, the immediate causes, however, are interarticular hemorrhage, comminution of the joint and secondary infection. A case of fracture of the base of the skull complicated by otitis media and mastoiditis and followed by bony ankylosis and hyperostosis is reported below.

Ankylosis may be due to the formation of fibrous bands which firmly connect the condyle with the articular fossa. This condition frequently follows comminution of the interarticular meniscus or its destruction by secondary infection. It generally allows moderate hinge movement, but no forward and lateral motion. The patient is able to masticate moderately, particularly if he makes an effort to prevent complete ankylosis by means of exercises.

In other types of mandibular ankylosis there is bony union and therefore complete loss of function. This may be the end result of fibrous ankylosis, but may also occur directly, especially in trauma resulting in fracture or comminution of the bony part of the joint in the presence of infection. Extensive hyperostosis may result, with firm attachment to the base of the skull, or with union of the ramus to the zygomatic arch, often including the coronoid process.

The onset of ankylosis is not always promptly recognized because its development is gradual, and is often overshadowed by more noticeable symptoms such as swelling of the face, fractures of the body of the mandible or base of the skull and secondary infection of adjacent parts. Infants may have mandibular ankylosis, which during the period of nursing from the breast or the bottle may be overlooked, often until much later when solid food is ordered.

When ankylosis is complete there is generally little difficulty in establishing a diagnosis, as the patient's chief complaint is a long-standing history of inability to open the mouth. Fracture of the condyle of recent origin, which often prevents free motion, can easily enough be ruled out. Muscular trismus, however, sometimes produces complete locking of the jaw (pseudoankylosis), and when it becomes chronic, as in cases of actinomycosis and myositis ossificans, may be mistaken for ankylosis vera. The commoner acute type of trismus of the masseter and internal pterygoid muscles is more easily differentiated. It is as a rule of very recent development, and is due to infection, particularly pericoronal infection around a partly erupted third molar. It is attended by pain, swelling at the angle of the jaw, painful deglutition and a rise in temperature. The x-ray easily discloses the condition. For the purpose of differential diagnosis it should also be remembered that the head of the condyle may be the seat of osteoma or chondroma. Such a case has been described by Ivy.[2]

In fibrous ankylosis the patient generally has slight motion, while in bony ankylosis motion is completely lost. The condition may occur bilaterally, but more frequently only one joint is affected. In cases of long standing the second joint may remain normal and retain its ability to function properly after operation on the affected side. If it is normal, the patient can push down the ramus slightly so as to create a small space between the molars, even if the other side is completely fixed.

In cases of ankylosis acquired very early in life the mandible remains markedly underdeveloped owing to lack of mastication. The chin recedes and the teeth are often crowded, so much so that the first permanent molars have insufficient room in which to erupt. The teeth also become carious and abscesses may form. Some patients are extremely undernourished, although it is remarkable how some of them, especially children, manage to push food into their mouths behind the last molars or through spaces created by the loss of deciduous teeth.

Ear deformities or the entire loss of the external ear are sometimes associated with childbirth trauma. I[3] have reported a case of this type elsewhere. When treating such cases it must be remembered that the muscles are either underdeveloped or atrophied if ankylosis occurs late in life. This accounts for the disappointing fact that after an arthroplasty has been performed the patient cannot open his jaw very wide. Daily exercises are indicated in such cases, and often a dilator must be used for a long period of time in order to accomplish the desired result.

Roentgen examination often gives valuable information, although the result may be disappointing on account of anatomic conditions. In cases where hyperostosis is excessive and where ankylosis with the base of the skull or zygoma is involved, good roentgen demonstration of the deformity is especially difficult. It is nearly always necessary to take exposures from various angles, and the anteroposterior as well as lateral positions

are needed. Sometimes stereoscopic pictures are of value.

The treatment of ankylosis is surgical. Severing of the fibrous connections in the joint is seldom successful, partly on account of the great depth of the condyle, which makes access difficult, and partly because this severance would hardly give permanent relief. Osteotomy at the neck of the condyle with arthroplasty often prevents reattachment, but only temporarily. The most satisfactory result is gained from osteoarthrotomy.

In performing an osteoarthrotomy a horizontal incision made over the zygomatic process and extended at right angles in front of the ear down to the tragus gives the desired exposure. The condyloid process is sectioned first, generally at its attachment to the ramus, at about the height of the mandibular notch. The condyle is then excised. If there is considerable hyperostosis the chisel has to be used to separate the bone from the base of the skull or from the zygomatic arch. If the coronoid process is involved the osteotomy must be performed in the upper part of the ramus, with separation and excision of both the condyloid and coronoid processes.

Case 8. The patient, a 6-year-old boy, was referred for examination because his head had ached several times during the previous week, and because he had had pains in the stomach and vomiting; he was unable to open his jaw and could not eat properly. The previous history

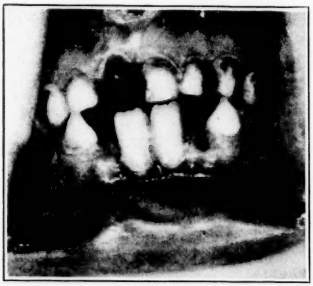

Figure 7. *Case 8. Before operation the patient was not able to open his jaw.*

was irrelevant. The boy had never been injured before or had previous trouble with his ears or jaw. The illness started 18 months previously, when he was knocked unconscious by an automobile. He was treated at a hospital for fracture of the left femur, which was somewhat comminuted; the leg was angulated and shortened. Soon after admission the patient developed an acute mastoiditis, which was operated on. A definite fracture of the skull, not visible in the x-ray picture, was discovered at operation. He was dismissed 2 months after the accident and was followed in the outpatient department, the last visit having been made 10 months previously.

The physical examination showed a thin, poorly developed and poorly nourished child; the skin was pale. He was unable to open his jaw. The right side was absolutely fixed; on the left side the teeth could be opened about 1.5 mm. (Fig. 7).

Roentgen examination showed a normal mandibular joint on the left, and bony ankylosis and hyperostosis of the condyle on the right (Fig. 8).

Figure 8. *Case 8. Ankylosis and bony hyperostosis of the mandibular joint. Osteotomy was performed between the white dots, and the bony mass was excised. C = enlarged condyle.*

The diagnosis was bony ankylosis of the right mandibular joint. Osteoarthrotomy was advised.

With avertin and ether anesthesia an incision about 4 cm. long was made along the zygomatic arch, and was extended by vertical incision in front of the tragus. After dissection of the skin flap the fascia was divided and the posterior attachment of the masseter muscle to the

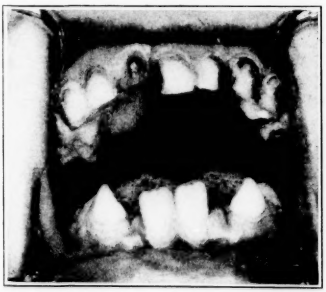

Figure 9. *Case 8. After osteoarthrotomy the patient could open his jaw freely and masticate well.*

zygomatic arch was severed. This brought into view the head of the condyle, which was found to be greatly enlarged and about the size of a pigeon's egg. When the capsule was opened, the articular surface was found solidly ankylosed to the glenoid fossa. The periosteum was

incised and the ramus was bared at the site of the attachment of the bony mass. Here an osteotomy was performed, the chisel being forced in an oblique direction from the middle of the mandibular notch down to the posterior border of the ramus (Fig. 8). The jaw could then be forcefully opened to about 2.5 cm. between the incisor teeth, after which it was freely movable. Next, the head of the condyle was excised, being separated from the base of the skull with a chisel. Its removal left a large space, which was partly filled with a piece of masseter muscle, turned over the cut-off part of the ramus and sutured to the internal pterygoid. A rubber drain was inserted to prevent hematoma. The fascia was sutured with catgut, and the skin with horsehair sutures.

The immediate postoperative condition was good, and the next day when the patient was examined it was found that he could open the jaw wide and without pain (Fig. 9). There was no facial paralysis. There was considerable local swelling about the wound but no infection. The drain was removed on the 2nd day. On the 4th day the patient developed a temperature of 103.5°F. without pain in the jaw or other symptoms, and on the 6th day the temperature was 104.5°F., when a diagnosis of acute follicular tonsillitis was made by a consultant. He received treatment and the healing progressed uneventfully from then on. He was given chewing gum to exercise his muscles the 1st day after operation, and when dismissed was much improved physically, owing to the fact that he ate well and could masticate his food. At a re-examination 2 months later, it was reported that he was eating well and without any discomfort. He had very bad teeth because he had not been able to clean them or have them filled while his jaw was ankylosed, and was referred to a dental clinic for treatment.

SUMMARY

Traumatic injury of the condyloid process frequently results from minor trauma, such as occurs from application of undue force when extracting teeth, or from careless use of the mouth gag under general anesthesia. This often causes an injury involving the joint capsule, or the meniscus, or both, and produces a weakness of the joint that may be associated with an audible noise when eating.

More severe injury may produce dislocation of the mandibular joint. Forward, backward and upward dislocations are distinguished. Diagnosis is made by clinical signs and x-ray examination. In forward dislocations the treatment is reduction, often under general anesthesia, to effect complete relaxation of the muscles, and the application of an appliance to limit motion for a few weeks. In case of backward and upward dislocations a rubber plate inserted over the teeth may be used to keep the condyle out of the joint fossa until the tissues have been restored to normal.

Fractures of the condyle occur more frequently than statistics indicate. In case of multiple fractures a collum fracture of the mandible may be easily overlooked. Careful x-ray examination from various positions is necessary for a complete diagnosis, as this fracture often is associated with forward, medial or lateral displacement of the neck of the condyle, or with medial or lateral dislocation of the head of the condyle.

The fracture can generally be reduced by manipulation under ether, after which intermaxillary ligation or the use of a splint is employed to immobilize the jaw. If there is marked displacement of the neck, or in cases of dislocation of the head of the condyle, open reduction may have to be resorted to in order to avoid malocclusion and associated masticatory difficulties. This is effected through an incision along the lower border of the zygomatic arch. The condyle can be pulled into position with a hook while the ramus is pressed down by an assistant.

In cases of traumatic destruction of the joint, or in untreated cases which have become ankylosed, osteoarthrotomy may be indicated.

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IMMEDIATE SURGERY IN ACUTE CHOLECYSTITIS

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IT IS apparent that surgical opinion regarding the delayed versus the immediate treatment of acute cholecystitis is gradually shifting toward the latter. The discussion has been revived from time to time by surgeons who disagree with the teachings of a previous generation that delayed operation is the treatment of choice, and who favor immediate surgery. Notable in this group are Miller,[18] Graham,[9] Eliason and McLaughlin,[7] Zinninger,[25] Stone and Owings,[21] Mentzer,[16, 17] Andrews[3] and Heuer.[11] We agree that immediate operation is the ideal procedure, not only because our clinical experience with it has been highly satisfactory, but also and more especially because we believe that the underlying diseased process demands immediate attention.

The term "acute cholecystitis" implies an infectious process in the gall bladder, and is therefore misleading. Most students of the pathology of this disease now agree that obstruction of the cystic duct is the primary factor and that infection — when present — is almost always a secondary phenomenon depending on obstruction for its development. Usually the obstruction is caused by a stone (Baumgartner,[4] Andrews,[3] Judd,[13] Hayes,[10] Zinninger,[25] Wilkie,[23] Lobingier[15]). In our experience a stone was impacted in the cystic duct in 28 of 29 cases. It is recognized, however, that obstruction may also occur as the result of edema arising from chemical irritation, for example, the regurgitation of pancreatic juice, or from edema caused by the lymphatics about the cystic duct, this lymphatic involvement being secondary to infection arising in the liver, the blood or the bowel. Allergy has recently been added by Alvarez[1] to the possible causes of edema in the region of the cystic duct. In general, however, it is true that in nearly all cases of acute cholecystitis the cystic duct is obstructed by a stone.

The anatomic relations of the cystic duct and the cystic artery, veins and lymphatics are such that obstruction to the duct inevitably involves to some degree the other structures at the root of the gall bladder. The cystic duct is naturally tortuous, and has numerous valves and papillary infoldings of mucous membrane in its lumen. We have repeatedly noticed that the artery leading to the gall bladder tends to take a short, straight course across the cystic duct to the gall bladder wall. During cholecystectomy, division of the cystic artery permits the tortuous folds of the cystic duct to be elongated, and to be elevated from 0.5 to 1 cm. The veins and lymphatics leaving the gall bladder are extremely numerous, and are much more closely associated with the cystic duct than is the artery.

Impaction of a stone in the cystic duct produces swelling about the stone, which in turn affects the lymphatics, the veins and the artery leading to the gall bladder. The pressure on these structures will vary in degree according to the anatomic structure in the given case. Edema arising from pressure on the lymphatics and veins is probably the earliest result of an obstruction in the cystic duct. As this edema persists and increases, further interference with the blood supply occurs, so that in some cases branches of the cystic artery are shut off. Complete occlusion of the cystic artery rarely occurs (Lobingier[15]), but if it does, complete gangrene of the gall bladder results.

The development of edema, necrosis, gangrene or perforation in the wall of the gall bladder is therefore immediately dependent upon the extent to which the blood supply of the gall bladder is involved by the swelling around the cystic duct. Denton[6] likened acute cholecystitis to a hemorrhagic infarct. The extent of the involvement of the gall-bladder wall varies according to whether large or small branches of the cystic artery are obstructed. Venous thrombosis is rare (Andrews[3]); the veins are usually dilated because of obstruction in the large venous plexus surrounding the juncture of the cystic and common ducts. Patches of gangrene and even perforation will occur as the edema, infarction and necrosis advance. Variations in the speed with which these changes occur after obstruction of the cystic duct appears will be pronounced, since the anatomic relations between the cystic duct, the artery and the veins are by no means constant.

There have been many studies of the bacteriology of acute cholecystitis, the outstanding ones in recent years being those made by Wilkie,[22] Denton,[6] Feinblatt,[8] Nickel and Judd,[19] Branch,[5] and most recently Andrews.[2] On one point all these investigators are in agreement; namely, that infection of the gall bladder is probably not the primary etiologic factor. Thus, Wilkie[22] showed that acute empyema followed intravenous injections of streptococci into animals when the cystic duct was obstructed, but failed to do so when it was patent. Nickel and Judd[19] found pathogenic bacteria (streptococci) in the majority of cases of acute

Presented at the annual meeting of the New England Surgical Society, Providence, Rhode Island, October 1, 1937.

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and subacute cholecystitis, while in the chronic cases, cultures taken from the gall-bladder contents were often sterile. Denton[6] has failed to demonstrate lesions primarily of a bacterial nature in acute cholecystitis, and concludes that mechanical and circulatory factors account for the majority of gall-bladder lesions. Feinblatt[8] holds that the role of infection as a cause of cholecystitis has been seriously overestimated. Branch[5] believes that the organisms recovered from infected gall bladders do not necessarily constitute the primary etiologic factor in the development of acute lesions. The more recent studies of Andrews[3] make it appear that the role of bacterial infection is indeed very minor. In quantitative studies he found as a rule no more bacteria in acutely inflamed gall bladders than in quiescent ones. Cultures taken from some of the severely damaged gall bladders were sterile. He states that in his experience empyema of the gall bladder has not been demonstrated by microscopic and bacteriologic studies. Denton[6] and Feinblatt[8] some years ago expressed similar ideas.

From the clinical point of view these findings are consistent with the course of many cases of acute cholecystitis. We have all operated on patients within forty-eight hours of the onset of pain and found gall bladders that appeared to be acutely inflamed; yet the fever, the white count, the general condition of the patient and the postoperative course were all consistent with a non-infectious lesion of the peritoneal cavity. In many respects the clinical picture of the early case of acute cholecystitis is identical with that of an early case of an ovarian cyst with twisted pedicle, and the course after operation in each case is much the same. Basically, the cause of these two conditions — an interference with the blood supply of an intraperitoneal viscus — is identical. In neither situation can the etiologic factor be considered a septic process.

If we agree that obstruction is first in the course of events in acute cholecystitis and is prerequisite to infection, it is obvious that immediate removal of the obstructed viscus before infection has occurred is the procedure of choice. The difficulties it presents are, first, the fact that in many cases there is a delay of several days before the surgeon is consulted, and secondly, that it is frequently impossible to decide from clinical study whether infection has been superimposed on obstruction.

Of the 29 patients with acute cholecystitis encountered since January 1, 1935, in private practice and in our service at the Massachusetts Memorial Hospitals, 1 was moribund on admission to the hospital, and died of perforation of the gall bladder and peritonitis. The other 28 patients were operated on either early or late, and all recovered.

It is impossible to say exactly what constitutes an immediate operation for acute cholecystitis. In theory, it is best to operate on most cases within forty-eight hours of onset, but in practice we seldom have an opportunity to do so. The profession as a whole has not yet reached the position of recommending immediate surgery in this disease. In 12 of our 29 cases operation was performed four days or less from the time of onset. In all these patients the convalescence was easy and comfortable. High fevers and serious reactions were absent, and complications did not occur. These cases did not react postoperatively in any way like cases of abdominal infection. In 11 of these 12 cases the gall bladder was removed. In 1 patient, who was very short and extremely fat, the gall bladder was merely drained because of the technical difficulties of removal caused by her obesity.

In 16 cases, operation was performed from five to fifteen days after the acute attack. All these patients recovered, but several had a stormy convalescence, and some had serious postoperative complications. As a group they impressed us strongly as being much sicker and having a much more difficult time than did the patients who were operated on soon after onset. We removed the gall bladder in 13 of these 16 cases; in the other 3 it was drained because of perforation and abscess formation around it.

In our experience the delayed operation of cholecystectomy is definitely harder than the early one. In both there is much edema about the cystic duct and cystic artery, and their identification is difficult. In the early operation, however, the edema is not so fully organized and there is a less firm inflammatory thickening of these structures.

The postoperative course in our group of delayed operations was complicated in 2 cases by wound infections that required long stays in the hospital, and in 1 case by a subphrenic abscess that necessitated rib resection and drainage.

Perforation and abscess formation had occurred in 4 of our 28 operated cases (14 per cent). This figure approximates the figures for gangrene and perforation reported by other men in recent studies of larger numbers of cases. Kunath[14] reports an incidence of 22 per cent and Heuer[11] one of 15.7 per cent. The high incidence of gangrene has not been sufficiently emphasized in the literature, and is a most important factor to be considered when deciding on the time for surgical treatment.

It had been our belief that stones in the common duct would rarely be found in acute cholecystitis,

since obstruction of the cystic duct was commonly present, and theoretically should prevent stones from entering. Among our operated patients, however, we found 5 who had stones in the common duct (18 per cent). Kunath[14] reports that 7 per cent of his acute cases showed them. Only 1 of our stone cases showed jaundice; there were, however, 4 other patients who had jaundice but no stones in the common duct. This demonstrates once again that neither the presence nor the absence of jaundice is significant in regard to stones in the common duct.

Edema about the junction of the cystic and common ducts was repeatedly noted in this group of cases. Andrews[3] believes that the slight jaundice seen in acute cases is caused by this inflammatory reaction and that this same phenomenon is responsible for the fever in certain cases of acute cholecystitis. He suggests that Charcot's intermittent fever may come from inflammatory obstruction of the common duct as well as from stones in it. In several of our patients who were operated on within forty-eight hours of the first pain, the gall bladder showed a tremendous increase in size, there was edema about an impacted stone at the junction of the cystic and common ducts, and there was a slight jaundice but no stone in the common duct. Immediate surgery in this type of case is safe, and will often rescue the patient from a long series of distressing complications.

We do not intend to enlarge upon the criteria by which to decide when to operate on late cases of acute cholecystitis. In the first place, we do not believe that specific data are available. All surgeons recognize fully that the pathology of this disease may be most deceptive, and that there is a very high percentage of error in correct diagnosis, particularly in the later stages. In general, our practice in late cases is to observe the patient for hours or days while giving him fluids and glucose. If we have evidence of spreading infection as suggested by a rising white-blood-cell count, a rising fever and a heightening pulse, we favor immediate drainage of the gall bladder. If it appears from our clinical impression and the above data that the infection is subsiding, we prefer delay and later operation.

SUMMARY

In this study of acute cholecystitis the advantages of the early operation have been emphasized. The basic lesion of acute cholecystitis is not infection, but obstruction to ducts and blood vessels, which produces edema, infarction and gangrene. The longer this process continues, the more chance there is for infection and its complications to develop. When the process can be interrupted by immediate cholecystectomy, infection rarely occurs, complications are few, and the final results are very satisfactory.

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DISCUSSION

DR. WALTER G. PHIPPEN, Salem: I wish to report a case of acute cholecystitis which was undoubtedly indirectly caused by trauma. A leather worker, aged forty-two, was crushed on his right side between heavy rollers. The immediate result was a ruptured right ureter with extravasation of urine, which filled the retroperitoneal space. This was drained in an appropriate manner. About ten days later the patient developed all the signs and symptoms of an acute cholecystitis, and at operation the gall bladder was gangrenous. The cystic artery had apparently been obliterated by pressure of the indurated edematous mass in the retroperitoneal space. The gall bladder was removed. Later the right kidney was removed and the patient made an uneventful recovery. Undoubtedly the cholecystitis was the indirect result of the trauma.

DR. FRANK H. LAHEY, Boston: Early operation has the additional advantage of permitting the correct diagnosis to be made in cases of acute pancreatitis that would be overlooked if operation were delayed. It is impossible at times to distinguish between acute pancreatitis and acute cholecystitis. In the beginning of our experience we felt as Dr. Clute did, that is, we tended to delay operation; but the more we see these patients the more we lean toward early operation. I believe that the trend in that direction, as indicated in the literature, is the result of the growing conviction that acute cholecystitis is somewhat, though

not entirely, similar to acute appendicitis. When patients can stand operation and the risk is justifiable, early operation is better than delay.

DR. LELAND S. MCKITTRICK, Boston: I should like to add a word concerning our experience with the six or eight diabetic patients we have seen who have come in with a stone impacted in the ampulla and a superimposed infection. Whereas we expect most of these conditions in non-diabetic patients to quiet down and permit more deliberate surgery, quite the opposite seems to be true in the patient with diabetes. With but one exception all this small group have gone on either to local perforation or to gangrene and empyema requiring drainage. In view of this we now feel that it is probably unwise to delay operation in such patients in the hope that an interval cholecystectomy may be done, but that it is probably better judgment to go ahead with operation as soon as the patient's carbohydrate metabolism and fluid balance have been brought to a point consistent with safe drainage of the gall bladder. It is apparently only the exceptional diabetic patient with an acute process who will be in good enough condition to permit removal of the gall bladder.

DR. ARTHUR W. ALLEN, Boston: The title of the paper, "Immediate Surgery in Acute Cholecystitis," seems to imply the possibility of emergency operations in the middle of the night and at variable intervals during the disease. A patient with an acute gall bladder may arrive at the hospital within forty-eight hours after the onset of pain, or four or five days after it. A great many patients arrive in such a distressing state, with dehydration, and so forth, that an emergency operation is extremely dangerous. If such a precedent is followed, the mortality will be high. I am sure Dr. Clute does not wish to imply immediate, but rather early, operation.

I believe that it is almost never necessary to operate on such patients in the middle of the night, as one might, for example, in a case of acute gangrenous appendix. If they are kept in the hospital for a few hours and their fluid balance is put in order, they are very much more likely to be in a relatively safe operable state than they would be if operated on as an emergency procedure. Furthermore, many patients whom we watch for a few hours and treat in a conservative manner are so much better by the next morning that I believe we can afford to delay and choose our own time for operation.

DR. JOHN HOMANS, Boston: I have learned something from this paper. Having always believed that acute cholecystitis was dependent upon the presence of a stone impacted near the outlet of the gall bladder, it has seemed to me very unlikely that a stone should also be present in the common duct even if the patient is jaundiced. However, I did see a patient the other day in whom I found small stones caught in the cystic duct, and who showed a type of acute cholecystitis rather different from the ordinary: in that case I now realize that the common duct might well have harbored a stone.

I was much interested to learn that the percentage of stones in the common duct in acute cholecystitis is so high. This is a factor which I have never before heard emphasized.

THE PRESENCE OF HEMOLYSINS IN ACUTE HEMOLYTIC ANEMIA

Preliminary Note

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WITHIN a period of four months we have observed 3 cases of severe hemolytic anemia characterized by acute onset, rapid development of profound anemia, fever, slight to moderate icterus and slight to moderate splenomegaly. In the first 2 cases, the blood picture showed high color index, increased mean corpuscular volume, macrocytosis and nucleated red blood cells. The resistance of the red cells to hypotonic salt solution was normal. In the third case, the blood picture corresponded to that commonly seen in congenital hemolytic icterus, namely, microcytosis, spherocytosis, increased erythrocyte thickness, and greatly increased fragility of the red cells to hypotonic salt solutions. Neither large daily doses of concentrated liver extract given parenterally in the first case nor repeated transfusions of blood in all the cases were of any therapeutic value. Splenectomy was, however, followed by prompt and dramatic response, complete recovery occurring in all 3 cases.

The hemolytic character of the anemia in these cases is demonstrated by the following laboratory criteria: bilirubinemia, absence of bile in the urine and increased urinary urobilinogen, together with the signs of greatly increased regenerative activity on the part of the bone marrow as evidenced by polychromatophilia, reticulocytosis, nucleated red blood cells, the presence of immature polymorphonuclear cells and hyperplasia of the bone marrow on direct examination at biopsy.

In performing compatibility tests with the serum of L. G. (Case 2), it was noted that hemolysis of the red cells of prospective donors frequently occurred. Numerous experiments were then performed which demonstrated the presence in the patient's blood serum of a hemolytic factor which was active against cells of all four blood groups,

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Read before the New England Pathological Society, November 18, 1937.

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normal control experiments being negative. On the appearance of the third case, tests for hemolysin again demonstrated the presence of a hemolytic factor active against the cells of all blood groups. The serum of the first case was then investigated and showed a similar, but weak, hemolytic activity.

METHODS

Fragility tests were done by the method of Daland and Worthley.[1] Urobilinogen was tested by the method of Wallace and Diamond.[2] The presence of hemolysins in the serum was determined by the following technic: 1 drop of fresh serum, 1 drop of a 5 per cent washed human red-cell suspension of the different isoagglutination blood groups and 1 drop of normal salt solution were mixed in 7-mm.-bore test tubes and allowed to stand at room temperature, or incubated at 37°C.*

Control observations using normal serums of various blood groups against the same red-cell suspensions were always made. In a few instances, the hemolytic titer of the serum was established by the following method: 0.5 cc. of 5 per cent suspensions of washed red cells, 0.5 cc. of 5 per cent guinea-pig complement, 0.5 cc. of serum in successive dilutions, and 1.5 cc. of normal salt solution were mixed in 7-mm.-bore test tubes and incubated at 37°C. for 1 hour.

Inactivation of serum was accomplished by heating in a water bath at 56°C. for 30 minutes. Complement was obtained from guinea pigs by heart puncture, the blood was allowed to clot and the serum was pipetted off. The blood serums, which were kept at icebox temperature for varying lengths of time, were frequently tested for hemolytic activity.

The simple experiments for hemolytic activity were varied from time to time: the serum was kept in contact with its clot for several hours at 5°C.; it was immediately chilled; it was mixed with human serum by the addition of 1 drop of homologous serum added to the hemolytic testing system.

CASE REPORTS

Case 1.† H. L., an ice-company supervisor, aged 50, was admitted to the Waltham Hospital on May 19, 1937, complaining of increasing fatigue and weakness. The family history was entirely negative. There was a past history of peptic ulcer 6 years before, and "intestinal grippe" 4 months before. One month previous to admission the patient felt fatigue on exertion, which rapidly gave way to increasing weakness. Then followed edema of the legs, vomiting of "bilious material" and the passage of dark-colored urine. The patient's physician gave him large daily doses of liver extract parenterally, but when he failed to respond he was sent to the hospital. On admission he was obviously in desperate condition with extreme pallor, moderate icterus and orthopnea. There was no abnormality of the tongue; the edges of both the spleen and the liver could be felt three to four fingerbreadths below their respective costal margins; there was moderate pitting edema of the lower legs; the neurologic examination, including that of the vibration sense, was entirely negative.

The laboratory data are recorded in Table 1. In brief they showed marked anemia, apparently of the macrocytic variety, leukocytosis, evidences of marked regenerative activity of the marrow (polychromatophilia, reticulocytosis, nucleated red cells and polymorphonuclear leukocytosis), and the chemical findings of a hemolytic type of

Table 1. *Record of Case 1.*

DATE	HEMOGLOBIN (100% = 15.5 GM.)	RBC	WBC	RETICULOCYTES	ICTERUS INDEX	REMARKS
1937	*per cent*	*millions*	*thousands*	*per cent*	*units*	
5-19						Transfusion, 750 cc. Fragility test, .42-.32. Concentrated liver extract 3 cc. (Lederle), daily intramuscularly.
5-20	43	1.63	18.4		30	MCD, 7.55 microns.
5-22	40	1.16	14.4	12		Transfusion 500 cc. Concentrated liver extract (Lederle), 6 cc. daily.
5-26	30	1.15		22		Transfusion, 500 cc.
5-27	30	1.40		22		
5-28	30	1.00		23		
5-31						SPLENECTOMY; transfusion, 950 cc.
6-1	41	1.82		20		
6-3	51	2.45		27	22	
6-8	56	2.77		17		
6-14	61	2.74		3.8		Transfusion, 500 cc.
6-17	74	3.62		1.2		
6-25	79	3.67		1.0	10	Liver extract (Lederle), 3 cc. daily.
9-3	71	4.08	11.2	1.0	17.5	
11-17	89	4.21	17.4	0.1		

icterus (bilirubinemia, lack of bile in the urine and much bile in the feces). Because of the patient's condition he was immediately transfused with 750 cc. of blood, and treatment with concentrated liver extract (Lederle) was continued in dosages of 3 cc. daily. The patient grew progressively worse, however, and even with two more transfusions and an increase in the dosage of liver extract to 6 cc. daily, he finally became almost moribund. Splenectomy was thought justified as an emergency procedure. Before the operation was performed, however, it was thought essential to do a sternal bone-marrow biopsy to rule out the rare possibility of hemolytic anemia due to malignant neoplasm. The biopsy showed extreme normoblastic hyperplasia, a picture differing strikingly from that of the megaloblastic marrow of pernicious anemia. Following two transfusions of blood on May 31, splenectomy under spinal anesthesia was done by Dr. H. Quimby Gallupe. The patient made a most dramatic and uncomplicated recovery, the erythrocyte count rising at first by about 200,000 cells daily. The spleen weighed 500 gm., and there were several large infarcts. The sections showed extreme congestion, extensive hemorrhages, thrombosis of veins and capillaries, and hemosiderosis, but no apparent proliferation of reticuloendothelial cells. In September, the patient presented the typical features of an attack of gallstone colic. In November, about 5 months after splenectomy, he was in excellent condition and ready to resume his occupation. The question of hemolytic activity of the serum was not investigated in this patient until more than 3 months after splenectomy, at which time a weak hemolysin was demonstrated.

Case 2.‡ L. G., a 38-year-old Italian-American housewife, was admitted to the Cambridge Hospital on July

*At the beginning of the studies in Cases 2 and 3, hemolysis took place almost immediately. Later, it took place within an hour or more at room temperature; finally, with the titer of hemolysins apparently diminishing, hemolysis occurred only after incubation at 37°C.

†This patient was seen in consultation with Dr. Leo G. Blacklow, to whom we are indebted for many courtesies.

‡We are indebted to the visiting physicians of the Cambridge Hospital for the opportunity of studying this case.

17, 1937, complaining of increasing weakness. The family history was essentially negative. In 1934 cholecystectomy had been performed at another hospital for cholecystitis and cholelithiasis. At that time evidence of slight anemia was discovered. The patient was followed in the outpatient department of this hospital, where diagnoses of "secondary anemia, cause unknown," and of hypothyroidism were made. Three weeks before entrance to the Cambridge Hospital she began to complain of weakness, which grew rapidly worse; in turn she developed dyspnea, palpitation and increasing pallor, and passed dark-colored urine. Examination on admission showed marked pallor with moderate icterus, a normal-appearing tongue, a large spleen extending three or four fingerbreadths below the left costal margin, and a negative neurologic examination. The laboratory data are recorded in Table 2. Except for the presence of a normal or somewhat diminished leukocyte count, the blood findings were almost identical with those of Case 1, and the urinary and blood chemical findings were those of a hemolytic type of icterus.

Table 2. *Record of Case 2.*

DATE	HEMOGLOBIN (100% = 15.5 GM.)	RBC	WBC	RETICULOCYTES	ICTERUS INDEX	UROBILINOGEN	REMARKS
1937	*per cent*	*millions*	*thousands*	*per cent*	*units*	*dilution*	
7-17	28	1.21	6.2				Gastric analysis — free HCl, 24 units. Conc. liver extract (Lilly), 3 cc. intramuscularly every 2 days.
7-26	20	1.00	4.8		25		
7-29		.97		20.8			MCV, 125 cu. microns. MCD, 7.44 microns. Transfusion, 500 cc.
7-30					22.5	1:80	Transfusion, 500 cc.
7-31							Transfusion, 500 cc.
8-2	30	1.28	6.2	10.4			Transfusion, 750 cc.
8-4		1.59	4.1	14.2			SPLENECTOMY; transfusion, 1200 cc.
	53	2.33	8.2	7.3			
8-9	57	3.75	15.0		10.0	1:40	Fragility test, .44-.32.
8-11						1:10	
8-16	55	3.06	16.8	9.7			Transfusion, 500 cc.
8-17					12.5	1:80	
8-19	57	3.82		8.8			
8-20					9.0		
8-23						1:40	
8-26	58	3.23	7.6	5.5	10.0	1:40	
8-28	49	2.79	11.5	8.2			Transfusion, 500 cc.
8-30	59	3.06	9.6	5.8	11.25	1:20	
8-31							Liver extract, 3 cc. $FeSO_4$, 1 gm.
9-4					7.0		
9-8	63	3.35	8.4				
10-4					10.0	1:20	Discharged. Fragility test, .44-.26.
10-7	66	4.13	9.4	3.9			
10-20	76	4.31					
11-17	85	4.78	6.9	1.3	6.25		Fragility test, .42-.20.

The patient was given two 3 cc. doses of liver extract (Lilly) intramuscularly, but showed no evidence of response. A bone-marrow biopsy revealed intense normoblastic hyperplasia without evidence of pernicious anemia. On July 29 the patient was transferred to the Beth Israel Hospital, where she was given four transfusions of blood in 5 days without definite effect on the blood picture or the clinical status. The hemoglobin ranged between 20 and 30 per cent, and the erythrocyte count between 970,000 and 1,280,000. Splenectomy was therefore performed under spinal and cyclopropane anesthesia on August 4, the patient receiving 1200 cc. of blood during the day. There was an almost immediate and dramatic recovery, although the postoperative course was complicated by consolidation of the left lower lung. Two more transfusions of blood were given when the blood picture showed some tendency to drop. On August 31 it was thought desirable to give parenterally 3 cc. of liver extract (Lilly concentrated) daily and iron in the form of ferrous sulfate, 1 gm. daily. Recovery continued uneventfully and on November 17, more than 3 months after splenectomy, the patient was in excellent physical condition and with normal blood findings.

In testing the patient's serum against the blood cells of prospective donors, it was noted that hemolysis frequently occurred. This was the occasion for testing the serum for hemolytic activity. A large number of experiments were performed as outlined above. These demonstrated in the serum a hemolytic factor which was active against red cells of all the blood groups, although in different degrees and with much individual variation (Table 4). Definite evidence for the presence of an autohemolysin was not demonstrated by the methods outlined above, but when the serum was allowed to remain in the icebox in contact with its clot for 48 hours there was evidence of some hemolysis.

The spleen weighed 500 gm. It was characterized microscopically by relative diminution in size of the Malpighian corpuscles, with marked increase in cellularity of the pulp and the presence of many large irregular cells and occasional giant cells with multiple nuclei (reticuloendothelial hyperplasia). Hemosiderin was greatly increased, and there was definite evidence of erythrophagocytosis. A study of impression preparations of the spleen gave evidence of myeloid activity, with many myelocytes and nucleated red cells. Extracts of the spleen, which are now being further investigated, showed definite hemolytic activity.

Case 3. G. C., a 44-year-old, married, Jewish housewife, with a negative family and past history, was admitted to the Beth Israel Hospital on August 27, 1937, complaining of weakness. She had been well until 5 days previously, when she had developed fatigue and malaise. On the

next day, pallor and fever had been noted; 2 days before admission she had become prostrated. She walked into the hospital ward, with assistance, but a few hours later was semimoribund with an extremely rapid pulse, a temperature of 103°F. and dyspnea. There was marked pallor, and moderate icterus. The tongue was normal; neither the liver nor spleen could be felt; the neurologic tracts of the spleen, which are now being further investigated, showed definite hemolytic activity.

In this patient's serum a strong hemolytic factor was found which corresponded closely in its reactions to that of Case 2. Hemolysis was induced with cells of all blood groups (Table 4), and in addition an autohemolysin was demonstrated. Upon the addition of 1 drop of homologous

Table 3. *Record of Case 3.*

DATE	HEMOGLOBIN (100% = 15.5 GM.)	RBC	WBC	RETICULOCYTES	NUC. RBC (PER 100 WBC)	ICTERUS INDEX	UROBILINOGEN	REMARKS
1937	*per cent*	*millions*	*thousands*	*per cent*		*units*	*dilution*	
8-27	22	1.51	20.1	20.6	36	37	1:80	MCV, 80 cu. microns. MCD, 6.4 microns. Cell thickness, 2.5 microns. Transfusion, 1150 cc.
8-28	34	1.90		16.1			1:60	Fragility test, .72-.44; hemoglobinuria; transfusion, 500 cc.
8-29								SPLENECTOMY; transfusion, 1700 cc.
8-30	36	2.12		16.7	82	27.5		
8-31								Transfusion, 500 cc.
9-2	43	1.93	24.7	10.0	60		1:80	Transfusion, 500 cc.
9-3	50	2.76	17.2	6.4		22.5		Fragility test, .74-.28.
9-9	31	1.75		15.5		22.5	1:40	
9-10								Transfusion, 500 cc.
9-11	38	2.02	31.5	17.7	30			
9-12								Liver extract (Lilly, concentrated), 3 cc. daily. $FeSO_4$, 1 gm. daily.
9-14				17.5				Transfusion, 300 cc.
9-16	42	1.75	15.2	17.0	41	35	1:20	
9-21	45	1.85		31.6		22.5	1:10	
9-27	47	2.15	11.7	20.8	18			
10-9	68	3.04	9.1	13.1		10		Fragility test, .70-.34.
10-10								Discharged.
10-26	71	4.00						
11-17	77	3.94	14.2	0.9		6.25		Fragility test, .44-.18.

examination was negative. The blood (Table 3) showed marked anemia, with polymorphonuclear leukocytosis and many normoblasts. The striking features of the blood picture were large numbers of very thick-looking microcytes (spherocytes). The fragility test was grossly abnormal; hemolysis began in a 0.72 per cent salt solution and was complete in a 0.44 per cent solution. The features of a hemolytic type of icterus were present. Seventeen hundred cc. of blood was given during the course of the day. The patient failed to respond, and indeed became worse. A severe transfusion reaction developed with the passage of large amounts of urine containing hemoglobin and with an increase in icterus. She was transfused again, however, on the following day, but since there was no change, either clinically or hematologically, splenectomy was performed under ethylene-ether anesthesia. There was immediate clinical response, with quick loss of the previous toxic appearance, a diminution in icterus and a fall in temperature. Several transfusions were given postoperatively; on two occasions it was noted that icterus became increased after transfusion. Convalescence was rather slow and was characterized by slight fever, continued anemia and many nucleated red cells in the peripheral blood. Because of the possibility that a depletion of maturation and other blood-forming substances might be occurring, 3 cc. of parenteral liver extract (Lilly, concentrated) and 1 gm. of ferrous sulfate were given daily beginning September 12. Convalescence occurred rapidly and the patient was discharged October 10. More than a month later (November 17), although she seemed clinically well, there was slight anemia and leukocytosis.

The spleen, which had been adherent to the diaphragm and therefore not palpable, weighed 360 gm. and microscopically showed extreme congestion of the sinusoids, without hemosiderosis and without evidence of erythrophagocytosis. The splenic corpuscles were well marked. Exhuman serum to the hemolytic test system described above, hemolysis was definitely inhibited.

With continued improvement after splenectomy, the hemolytic factor gradually became diminished, the spherocytes gradually disappeared and the fragility test finally became normal.

SUMMARY OF CASES

All the patients became acutely ill, with weakness as the outstanding symptom. In Case 3 the course was a precipitate one. Anemia developed rapidly and was associated with moderate icterus. The spleen was readily felt in the first 2 cases. Since pernicious anemia was the initial diagnosis in those cases, it was of interest to note the normal appearance of the tongue, the absence of neuro-

Table 4. *Summary of Tests for Hemolytic Activity of Suspected Serums.*

SERUM	BLOOD GROUP OF PATIENT'S SERUM*	BLOOD GROUP OF TESTING CELLS	NUMBER OF EXPERIMENTS	NUMBER WITH POSITIVE HEMOLYSIS
Case 1	O	AB	0	—
		A	1	0
		B	2	0
		O	3	1
Case 2	O	AB	9	7
		A	11	5
		B	12	4
		O	19	6
Case 3	B	AB	7	3
		A	20	13
		B	20	10
		O	35	22

*International nomenclature. Blood Group O=Type IV Moss; A=Type II Moss; B=Type III Moss; AB=Type I Moss.

logic phenomena and the presence of free hydrochloric acid in the gastric juice. The blood picture was similar in the first 2 cases, being characterized by the presence of polychromatophilic macrocytes and an increase in the mean corpuscular volume, but by a normal, average red-cell diameter. Microcytosis was not striking, and the fragility test was normal. In the third case, spherocytosis (the presence of thick microcytes) was outstanding and was associated with a grossly abnormal fragility test. The jaundice was of the hemolytic variety, with increased bilirubin of the indirect variety, acholic urine and increase in urinary urobilinogen.

In none of the cases were transfusions of any benefit. In fact, on several occasions the reverse was true, definite evidence of increased blood breakdown occurring after transfusion. An adequate trial with large doses of parenteral liver extract in Case 1 failed to show any therapeutic results. Splenectomy performed as an emergency measure, with the patient in each case semimoribund, produced immediate therapeutic effect.

Experiments for hemolytic activity of the serums in these cases demonstrated the following (Table 5): pronounced hemolytic activity against cells of all blood groups, including those of Group O; definite evidence of autohemolysis in Case 3; inactivation of hemolysis by heating the serum to 56°C., with re-establishment of activity upon the addition of guinea-pig complement; increase in hemolytic activity of the serum when it was kept at icebox temperature overnight; gradual diminution in hemolytic activity with prolonged standing at icebox temperature; diminution of hemolytic activity when the serum was incubated with its clot; suppression of hemolytic activity upon incubation at 37.5°C. with normal human serum before the red cell suspension was added; incomplete inhibition of hemolysis when the serum was mixed with normal human serum and allowed to stand at room or icebox temperature before addition of the testing cells; and finally, an individual variability in the hemolytic susceptibility of cells from different subjects of the same blood group.

Table 5. *Summary of Characteristics of Hemolytic Activity of Serums (Cases 2 and 3).*

STATE OF SERUM	BLOOD GROUPS OF RED CELLS TESTED			
	AB	*A*	*B*	*O*
Fresh serum	H	H	H	H
Fresh serum — after incubation with normal human serum	O	O	O	O
Fresh serum — after standing at 5°C. for 15 hours	H+	H+	H+	H+
Fresh serum — after prolonged standing at 5°C	H−	H−	H−	H−
Heated serum — 56°C. for ½ hour	O	O	O	O
Heated serum — after addition of guinea-pig complement	H	H	H	H

In all experiments 1 drop of serum, 1 drop of normal salt solution, and 1 drop of a 5% suspension of red cells were used.
H = hemolysis.
O = no hemolysis.
H+ = hemolysis more marked than with fresh serum.
H− = hemolysis less marked than with fresh serum and gradually diminishing.

The microscopic picture of the spleen differed in all 3 cases, congestion and multiple thromboses being present in Case 1, reticuloendothelial proliferation and erythrophagocytosis being the outstanding features of Case 2, and simple congestion of the pulp characterizing Case 3. Extracts of the spleen were made in Cases 2 and 3, and various fractions showed a marked hemolytic quality.

DISCUSSION

Since 1925, the date of Lederer's first report on "acute (febrile) hemolytic anemia,"[3] over 50 cases of this syndrome have been reported. In 1909 Chauffard and Vincent,[4] in a thorough study almost completely neglected in the literature, described under the title "Hémoglobinurie hémolysinique avec ictère polycholique aigu," a case of acute hemolytic anemia corresponding clinically and hematologically in every respect to what is now frequently called Lederer's anemia. What is more, Chauffard and Vincent demonstrated in their case the presence of a very active hemolysin in the serum, which was "precocious" in type, intense in action, not secondary to blood destruction but apparently the cause of it, and of endogenous origin. It appears that in none of the cases of acute hemolytic anemia reported since the work of Chauffard and Vincent has an hemolysin been investigated, although some speculations have been made regarding its presence, and regarding the possible antilytic value of blood transfusion. In a few cases, an autoagglutinin has been found.

Our own findings are quite similar to those of Chauffard and Vincent, although because of present-day knowledge of the blood groups we have been able to extend them. The unusual activity of the hemolysins, which appear to be of endogenous origin, and which were found to possess a strong lytic action upon cells of their own type as well as upon those of Group O, serves to set them apart from the known isohemolysins. The latter are occasionally discovered in the course of isoagglutination compatibility tests done prior to transfusion. We have observed 2 such cases. As Wiener[5] points out, isohemolysins of this type correspond in specificity to the isoagglutinins normally present in the serum. The commonest isohemolysin is of the alpha type, and is usually present in Group O serum, which contains alpha and beta agglutinins (and hemolysins). So far as we are aware, no hemolysin has yet been reported which is active against Group O cells, which indeed are theoretically incapable of being hemolyzed by isohemolysins.

The antilytic action of normal human serum as demonstrated in our experiments may have some bearing upon the therapeutic value of blood transfusions, which have usually been curative in acute hemolytic anemia albeit in several cases splenectomy has been required. The gradual diminution in activity of the hemolysins, with continued recovery of the patients, makes possible a causal relation between the hemolysin and the development of the hemolytic syndrome. The presence of large numbers of spherocytes in Case 3, with their subsequent diminution in association with diminution in titer of the hemolysin, indicates that the spherocytes and the hemolytic factor were closely related. In other words, it is possible that the hemolysin was the direct cause of the development of spherocytes. Certain experiments which will form the basis of another paper tend to confirm this speculation.

Acute hemolytic anemia may be related to paroxysmal (cold) hemoglobinuria, to paroxysmal nocturnal hemoglobinuria (Marchiafava[6]), to acquired hemolytic icterus,[7] to hemolytic splenomegaly (Banti[8]) and even to congenital hemolytic jaundice. Studies now in progress in the latter disease have demonstrated hemolysins in 2 cases.

Although most cases of acute hemolytic anemia appear to respond effectively to transfusions, occasional cases, it must be remembered, are so severe that the more radical measure of splenectomy must be employed. This may be a life-saving measure.

SUMMARY

In 3 cases of acute hemolytic anemia failing to respond to transfusion but responding dramatically to splenectomy, hemolysins of unusual activity were demonstrated. Since the hemolysins were active against red cells of Group O and their own type, they fail to correspond to any hitherto described hemolysin. Furthermore a hemolytic factor was demonstrated in splenic extracts of 2 of the 3 cases.

From this preliminary paper no definite conclusions can be drawn; but the evidence already at hand suggests that the hemolysin was causally related to the development of the disease, that it was of endogenous origin, and that it was the causative factor for the presence of spherocytic microcytes in the third case. These hypotheses are now under investigation.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 24021

PRESENTATION OF CASE

First Admission: A fifty-six-year-old Italian housewife entered the hospital because of left flank pain of one day's duration.

On the day before entry she rather suddenly developed steady aching pain in the left lumbar region which spread forward to the left lower side of the abdomen but not down to the genitalia. She felt feverish, but had no chills. She had no bloody urine, frequency, dysuria or other urinary symptoms.

For the previous ten years she had moderate dyspnea on exertion and moderate orthopnea, so that she used three pillows while sleeping. She had no edema, chest pain, cough or hemoptysis, but did have occasional night sweats. She took ten drops of a brown alcoholic medicine three times a day for this "heart trouble." Her past history was otherwise negative. Her family history was noncontributory.

Physical examination revealed a feverish, rather obese woman apparently suffering some pain. Her heart was enlarged to the left, 1 cm. beyond the left midclavicular line. The rhythm was grossly irregular, and there was a diastolic apical murmur with a loud first sound. The apex rate was 100 and the radial rate 92. The blood pressure was 120 systolic, 80 diastolic. The abdomen showed moderate left lower quadrant and left costovertebral tenderness.

The temperature was 100°F., the pulse 92. The respirations were 20.

The urine had a specific gravity of 1.014, contained 4 white cells per high power field, but was otherwise negative. The blood showed a red-cell count of 4,500,000 with 90 per cent hemoglobin and a white-cell count of 14,800. The urine culture was negative.

X-ray of the abdomen showed the left kidney markedly enlarged and the right kidney fairly small. There were no unusual areas of calcification visible in the region of the kidneys. An intravenous pyelogram showed that the dye was excreted promptly by the right kidney and not at all by the left. The right kidney pelvis, calices and ureter appeared normal. A retrograde pyelogram showed no evidence of disease in the left kidney pelvis and calices.

For the first week after entry the temperature remained elevated, fluctuating between 100 and 102°F., but on the eighth day the chart became flat. On the fifth day a urine culture contained *Bacillus coli.* On the tenth day another intravenous pyelogram showed the same findings as before. A chest plate showed the transverse diameter of the heart definitely increased. There was also increase in size across the base, but the greatest prominence was downward to the left in the region of the ventricle. She was discharged on the fifteenth day.

Second Admission (five days later): She felt well for four days after discharge, except for slight burning on urination. On the fifth day, while urinating, she suddenly had a very severe pain in her right costovertebral angle and re-entered the hospital two hours later.

Physical examination revealed marked right costovertebral tenderness. The heart findings were essentially the same as on the previous entry, and her blood pressure was 120 systolic, 90 diastolic.

The temperature was 100°F., the pulse 96. The respirations were 20.

The blood gave a red-cell count of 4,690,000 with 70 per cent hemoglobin, and a white-cell count of 28,900, 98 per cent polymorphonuclears. An x-ray of the abdomen revealed no appreciable change from the previous examination. The costovertebral pain persisted and she remained completely anuric until the third hospital day, when she passed about 200 cc. of urine which showed a specific gravity of 1.012 and a trace of albumin. It contained many white cells, but no red cells or casts. By that time she had become somewhat drowsy and was vomiting occasionally. Her temperature had risen to 102°F., and her white-cell count to 42,000. On the following day the nonprotein nitrogen of the blood was 87 mg. per cent. Her temperature fell to normal, where it remained until death, and her white-cell count fluctuated between 14,000 and 28,000. On the fifth day she passed no urine, but on the following day catheterization produced 1300 cc., which showed a specific gravity of 1.010 and a slight trace of albumin. It contained many white cells and from 5 to 10 red cells per high-power field, but no casts. The stool on that day gave a 3+ guaiac test. Her condition had improved somewhat, and she appeared to be mentally clearer. However, on the seventh day her nonprotein nitrogen was 105 mg. per cent. She passed about 500 cc. of urine on that day and about 600 cc. on the following day. On each day the urine had a specific gravity of about 1.012 and contained albumin; there were many white cells, but no red

cells or casts. For the last three days she was in coma, and she died on the tenth hospital day.

Notes on the History

Dr. Richard C. Cabot: We have then, from the history alone, a person with a cardiac history of ten years who, though she has not been very well, seems to have been well enough to get around up to the very day before she came here, when she suddenly had pain in the left flank. That is all we know. The question is whether we can connect these two things.

The urine was negative, and of especial interest is the fact that it contained no blood. The x-ray examination showed a fairly small right kidney. I take it they did not mean that it was abnormally small. "There were no unusual areas of calcification visible in the region of the kidneys." In other words, there is no reason to think of stones.

One of the questions we have to consider is why she was discharged, in view of the fact that she died so promptly soon after. My guess is that they did not have much to offer in the way of treatment, and that the patient was restless and wanted to go home.

At the second admission she had pain in the *right* costovertebral angle. Nothing is said about pain in the left side at this time. The white-cell count was 28,000. You remember that it was 14,000 at the last admission.

The most important thing we have to face is the fact that she was in the hospital three days and passed no urine.

Differential Diagnosis

This is a ten-year cardiac story with no cardiac symptoms. There was no edema, and nothing in the lungs. Her heart was doing fairly well in spite of absolute arrhythmia. First she had left-sided and then right-sided severe pain, associated with anuria, pyuria and a rising leukocyte count. The only sure thing in any other part of the body is the guaiac test which showed something in the intestine; otherwise we have nothing to call attention to any other organ except the heart and the kidney.

Let us consider the heart. Here is a woman of fifty-six, an Italian; that means she is older than most people of our race at that age. She has a heart that may perfectly well be that of mitral stenosis and could conceivably be due to other types of disease, but they are not so probable, I should say. Her heart is enlarged, especially the base and the left ventricle, and she has what is called a diastolic murmur, not further characterized, at the apex, a sharp first sound and absolute arrhythmia — those things fitting together to make us think of mitral stenosis. It is queer, at fifty-six, that she had had no symptoms until within ten years, but of course not at all unprecedented.

If it was not mitral disease, what could it be? She has low blood pressure. There is nothing to suggest the hypertensive types of heart trouble. The heart was not so much enlarged as one would suppose it would be if she had had hypertension.

Now that certainly is not the whole of it. She also has had night sweats from time to time. If she were French, I should think less of that — French people have night sweats a good deal of the time without any good reason that I can think of. The night sweats suddenly link up with the fever she had here on two occasions. The fever, however, was not lasting. In both cases the temperature flattened out. Nothing makes us think of tuberculosis of the kidney, except the fact that the organ is enlarged. She never passed pus. She has never had the bladder symptoms that usually go with a tuberculous kidney. We have nothing to make us think of malignant disease or cystic kidney, which is ordinarily bilateral. Embolism — first left and then right — seems to be the only thing one can say, and the only thing that displeases me is that it is so plain. Long experience has taught me that if a diagnosis is perfectly easy, it is usually wrong. I doubt if I can do better than that, however. It seems to me that she had embolism first of the left and later of the right kidney, and died from anuria subsequent to the shutting off of kidney function. There is no evidence of nephritis. I see no reason why we should think of that from anything given here.

Were the emboli septic or were they bland? They could be bland from a ball thrombus in the left auricular appendage with mitral stenosis, and we certainly can have fever and leukocytes with bland emboli. On the other hand I have never seen a blood-leukocyte count of 41,000 with bland emboli, and it seems to me that the suddenly increasing white count suggests that the emboli were septic. Septicemia was not the main cause of the death, however, it seems to me, but rather the cutting off of the blood supply and suppression of kidney function secondary to it. But at least septicemia, if there was one, helped.

I should suppose, then, that there had been a bacterial endocarditis on the mitral valve, not elsewhere in the heart. I suppose there was an old mitral stenosis back of that. The heart was not greatly enlarged, only moderately, as we should expect with mitral disease. I see no reason to suppose anything wrong in the lungs or other organs except the kidneys. But there is one problem that bothers me. If she is throwing septic emboli into the kidneys, why not somewhere else? I cannot answer that. It is against my diagnosis. However,

it does not seem enough to suggest any alternative diagnosis. There may have been an embolus in the intestinal tract, though we have nothing but a guaiac test to back that up. In these cases at postmortem we often find emboli in various organs although there was no suggestion of them during life. If there were emboli in the kidneys, I believe there were emboli elsewhere. Whether the autopsy was complete enough — Dr. Mallory has told me that it was not complete — to show that, I do not know. I do not believe she would throw them only into the kidneys. The best diagnosis I can make is bacterial endocarditis on top of old mitral stenosis, with embolism, certainly septic embolism, of both kidneys.

Dr. George W. Holmes: This x-ray film shows a distinct difference in the size of the kidneys. The left is nearly twice the size of the right. It is not particularly abnormal in shape. There is a suggestion at the border of a slight amount of lobulation, but it is not the kidney of cystic disease or tumor. With the intravenous dye there is evidence of non-function. We have then a large non-functioning kidney on the left with a normal kidney on the right. When the retrograde pyelogram is taken we find no dilatation of the kidney pelvis, no dilatation of the calices and no evidence of obstruction in the ureter. We now have a non-functioning kidney not due to obstruction in the ureter or pelvis, with no thinning of the cortex of the kidney such as one would expect with hydronephrosis. When we study the outlines of the calices and the pelves I should say they were normal — not enough variation to make a diagnosis of tuberculosis or even pyelitis, although I know that pyelitis may exist without x-ray evidence. We shall have to explain this absence of function on something very similar to what Dr. Cabot has suggested.

Dr. Cabot: How about the right kidney? At the second entry she had pain on the right.

Dr. Holmes: We have no examination at the time of the second entry; so far as I can tell, it was normal at the time of the first.

Dr. Fuller Albright: I saw this patient only on the second admission. The one thing that disturbed us was why she had emboli going to both kidneys and nowhere else. We developed a fantastic theory about that. We thought that she had emboli to the left kidney first, which caused thrombosis of the left renal artery, and which subsequently backed up into the aorta and extended over into the opening of the other renal artery. We felt that she did not have bacterial endocarditis. We thought the emboli were aseptic. As a matter of fact she had a blood culture that was negative, I believe.

Clinical Diagnoses

Rheumatic heart disease with mitral stenosis and auricular fibrillation.
Bilateral infarction of the kidneys.
Uremia.

Dr. Cabot's Diagnoses

Old mitral stenosis probably with bacterial endocarditis.
Septic emboli in both kidneys.

Anatomic Diagnoses

Bland emboli to both renal arteries.
Bilateral renal infarction.

Pathological Discussion

Dr. Tracy B. Mallory: I think one of the difficult things in these clinical discussions is to bring oneself to make a diagnosis that seems obvious, and I might say that on years of experience Dr. Cabot is one of the few who has consistently had the courage to do that. The diagnosis was primarily what he suggested — bilateral renal embolism. We found multiple infarcts of varying ages in both kidneys, the ones on the left being distinctly older than those on the right, but within each kidney there were infarcts of somewhat varying age.

Unfortunately the autopsy was limited to the abdomen so we could not see what the heart valves showed. Whether there was a bacterial endocarditis or simply an old rheumatic stenosis, we could not check with certainty. We could see from examination of the kidneys that these emboli were certainly not frankly septic. In other words there could not have been a bacterial endocarditis with a pyogenic organism such as a streptococcus or pneumococcus. I think we can guess a little further and say that it was probably not a bacterial endocarditis. In the kidney tissue between the infarcts, and there were a significant number of uninfarcted areas, we did not find the lesion which is so characteristic of *Streptococcus viridans* endocarditis, so-called embolic nephritis with individual glomerular lesions. That does not absolutely rule out bacterial endocarditis; it simply is of inferential value.

We were surprised at the autopsy — as Dr. Cabot and Dr. Albright were from the clinical course — that there was no evidence of embolism elsewhere. We did not have permission to examine the head, but the spleen, the other abdominal organs and the gastrointestinal tract were all entirely negative, and the only evidence of embolism that was found was in the kidneys.

DR. BRAILEY: Is it not peculiar that she had these two dramatic episodes of pain and that the kidneys should shut down on the basis of multiple emboli?

DR. MALLORY: We have seen pain and complete suppression of urine with renal infarcts before. I think they usually have been very massive ones. We have, I am sure, seen a white-cell count go as high as 40,000 with bland infarction.

DR. CABOT: There was no embolus in any of the big vessels?

DR. MALLORY: One large embolus was found lying nearly free in the right renal artery, but it had not completely occluded it. On both sides there were multiple occlusions of small arteries.

A PHYSICIAN: What was the explanation of one kidney being so much larger than the other?

DR. MALLORY: That was at the first examination, when only the one kidney was involved.

DR. CABOT: At autopsy they were nearly the same size?

DR. MALLORY: Yes.

DR. CABOT: And both large?

DR. MALLORY: Yes.

CASE 24022

PRESENTATION OF CASE

A twenty-four-year-old white Greek housewife entered the hospital with a complaint of cough and fever of nine days' duration.

Nine days before entry she awoke in the morning with a headache and dizzy feeling. During the day she felt feverish and passed frequent, small amounts of cloudy urine. That evening she had a severe chill and perspired profusely. Her physician examined her urine and told her she had an infection in her kidney. He gave her some pills, and her condition improved somewhat in the next few days. The urinary symptoms lasted three or four days. The temperature continued to be elevated and she had mild intermittent pain just under the left ribs. Six days before entry she began to have moderately severe, sharp, pulsating pain in the lower right anterior chest which was not influenced by breathing. The following morning she developed a dry cough and sore throat. Her fever increased and she soon began to raise dark black tenacious sputum, which was not blood streaked. The day before admission she developed a "fever blister" on her upper lip, and she also became somewhat dyspneic. She had had her last menstrual period seven weeks before entry and in the weeks before entry had some morning nausea and vomiting.

The family history was negative except that one brother had tuberculosis and was in a sanatorium. She had very infrequent colds and no previous cardiorespiratory symptoms. Nine months before entry just after the birth of her second child she had urinary symptoms lasting a week similar to those in her present illness. She had had two normal pregnancies, the first child dying of "meningitis" at the age of eight months. The past history was otherwise negative.

Physical examination revealed a well-developed, well-nourished, not acutely ill, somewhat dyspneic, perspiring female. Examination of the chest was negative except for increased voice sounds in a small area posteriorly between the angle of the scapula and the lower dorsal ribs on the right. The blood pressure was 120 systolic, 90 diastolic. Pelvic examination revealed bluing of the introitus and a soft patulous cervix.

The temperature was 103°F., the pulse 120. The respirations were 24.

The urine had a specific gravity of 1.010 and contained 5 to 10 white cells per high-power field in the sediment. The blood showed a red-cell count of 4,270,000 with 80 per cent hemoglobin. The white-cell count was 20,200, 84 per cent polymorphonuclears. No tubercle bacilli were found in the sputum on repeated examination, and the stools were negative. The blood-serum chlorides were equivalent to 87 cc. N/10 sodium chloride. Blood cultures were twice negative, and a sputum culture contained many hemolytic streptococci. A blood Hinton test was negative.

An x-ray of the chest revealed an area of cloudy consolidation in the second right interspace, particularly around the hilus. The lung fields were otherwise clear. The costophrenic angles were clear, and the heart was not remarkable.

On the day after entry the temperature rose to 105°F. and the respirations to about 40. She became slightly cyanotic and was put in an oxygen tent. On that day she had an attack lasting about ten minutes in which she became disoriented and moved her right arm convulsively. The temperature at the time was 106°F. For the next week the temperature remained high, never falling below 101 and often rising to 105°F. On the fourth day she complained of headache, stiffness of the neck and some inability to use the right leg, but no reflex changes. Examination of the chest was essentially the same as before. On the following day she suddenly began to pass red blood and clots from her vagina. She bled freely, but her general condition remained unchanged. After a few hours she expelled an intact placenta and was immediately given pituitrin and ergot. The blood pressure remained unchanged and the bleeding lessened considerably. On that day she had another cerebral attack similar to the previous episode and lasting a few minutes. Her head turned to the right, her eyes rolled about, and her right arm

moved in tonic contractions. However, she did not lose consciousness. Neurological examination revealed no cranial nerve involvement. The neck was moderately stiff, but the Kernig was negative. There was marked weakness of the right arm with decreased activity of its reflexes. No sensory changes could be made out. A lumbar puncture was performed, but only a few cubic centimeters of bloody fluid could be obtained. The respiratory and pulse oscillations were fair, and the initial pressure was 150. The spinal fluid contained 25,000 red cells and 2100 white cells per cubic millimeter, with 68 per cent polymorphonuclears and 32 per cent lymphocytes, 198 mg. per cent of protein and 38 mg. per cent of sugar. No tubercle bacilli or other bacteria were seen on direct smear.

Three days later, on the ninth hospital day, she became somewhat drowsy, her neck became stiffer, and the Kernig was positive. Otherwise, the neurological examination was essentially the same as before. A lumbar puncture yielded only 1 or 2 cc. of bloody fluid. The vaginal discharge, which had been scant, increased in amount and became foul smelling. The blood at that time showed a red-cell count of 3,650,000 with 60 per cent hemoglobin. The white-cell count was 19,500, 90 per cent polymorphonuclears. An x-ray of the chest the following day showed the area of increased density in the region of the right hilus to be slightly smaller than before, and its upper portion seemed somewhat less dense, suggesting cavitation. Neurological examination revealed that she had developed a definite right facial lesion of the central type. She was started on prontylin in a dosage of 80 gr. daily, and the temperature dropped quite sharply to 99°F., without change in pulse or respirations. However, it rose slightly the next day, and the following day, which was the eleventh hospital day, it reached 104°F. It remained at about that level until death. The serum chlorides of the blood were equivalent to 98 cc. of N/10 sodium chloride. The carbon-dioxide combining power was 44.5 vol. per cent. On the thirteenth hospital day she developed a right external strabismus, and her right leg became flaccid. She was given a clysis of 1000 cc. of 2.5 per cent dextrose in saline with 100 cc. of prontosil, and on the following day a clysis of 1000 cc. of dextrose and saline with 200 cc. of prontosil. She died that day.

Differential Diagnosis

Dr. Alfred O. Ludwig: The onset of this patient's illness certainly suggests that she had some acute infectious process, since it was marked by headache, fever and chills, as well as by sweating. The urinary symptoms and her physician's statement of the examination of the urine would lead one to believe that he was correct in making the original diagnosis of a urinary infection. This might well have been pyelitis and cystitis. Three days after the onset we first hear of chest pain situated in the right anterior chest, and this, as it is recorded here, does not suggest a pleuritic type of pain since it was not associated with breathing. One wonders whether possibly the pain was associated with something under the diaphragm, with a rather unusual reference of pain to the lower anterior chest. Soon afterward the patient began to develop respiratory symptoms in the nature of cough and sore throat. The development of herpes would be consistent with almost any infection associated with high fever, but is perhaps more commonly seen with the high temperatures during the course of pneumonia and very often with meningococcal meningitis. The onset of dyspnea also suggests that there has been some extension of the process to the patient's chest. The menstrual history associated with what we learn later in the history makes a diagnosis of pregnancy quite evident.

In the patient's past and family history it is significant that she had one brother who had tuberculosis, but we are not told whether she was in contact with him. It is interesting that the patient also had urinary symptoms after the birth of her second child, nine months before this illness. It would seem quite likely that this may also have been a pyelitis, and it is known that patients who have a pyelitis during pregnancy not infrequently have a recurrence with subsequent pregnancies. It might also lead one to think that in addition to the pyelitis there might actually have been some pyelonephritis, but I do not believe that this had led to any serious impairment of kidney function. We should like to know more about the exact cause of death of her first child — what the nature of the meningitis was. If this had been tuberculous it would be of considerable importance in the differential diagnosis of the patient's illness.

Physical examination tells us that we have a patient who was probably suffering from some acute infection involving her lung, and the finding of an area of increased voice sounds on the right side leads one to believe that there was a small area of consolidation there. Pelvic examination confirms the diagnosis of pregnancy.

A finding of 5 to 10 white cells in the urinary sediment in a female patient is not of significance unless the specimen was obtained by catheter. It is perhaps of note that the specific gravity was only 1.010; unless the patient had been forcing fluids one would expect that with the high fever and profuse sweating the urine would be quite concentrated. The red-cell count indicating a slight anemia and the leukocytosis with the predomi-

nance of polymorphonuclears in the smear are consistent with infection. I believe that the absence of tubercle bacilli in the sputum on repeated examinations almost certainly rules out tuberculosis as a cause of her pulmonary symptoms. The blood chloride value of 87 cc. N/10 sodium chloride tells us that the patient's chlorides were depleted, probably due to chloride loss from excessive sweating. I do not know whether one can lay too much significance on the finding of hemolytic streptococci in the culture of the sputum, as these are very frequently found, even in the throats of normal individuals.

According to the radiologist, the x-ray findings of the area of consolidation around the right hilus and also clouding of the whole right lower and middle lobe are indicative of infection in the lung. The findings do not suggest infarct, as this lesion is usually found in the periphery. Tumor is a possibility, but the radial markings extending out into the lung field from the hilus shadow are not those typically seen in cases of malignancy.

Subsequently, the patient became progressively worse, with an increase of temperature and respirations, cyanosis, and the appearance of a new symptom, namely an attack of disorientation and convulsive movements limited to one side of the body and at first only to one arm. This episode was apparently associated with a marked increase in temperature to 106°F., and from that time on the temperature took on an irregular or septic type of swing. We then note evidence of meningeal irritation with headache and stiffness of the neck. At this point the patient's pregnancy was spontaneously terminated, as evidenced by the passage of blood and clots by the vagina. If the dates are correct, one would not expect a placenta to have developed, and I should say that the statement that an intact placenta was passed should have read "an intact ovum was passed." The occurrence of abortion under these circumstances is not at all unusual, in fact in pneumonia associated with pregnancy the usual course is abortion during the course of the infection. The patient then had another cerebral attack, with her head turning to the right and with convulsive movements of the right arm. The localizing symptoms we have had in connection with her neurologic lesion have all pointed to the left motor cortex. At this time we again note stiffness of the neck and also weakness of the right arm. Lumbar puncture, while its results are somewhat unsatisfactory, is of considerable help in establishing the nature of the lesion. The initial pressure was within normal limits, and respiratory and pulse oscillations were normal. So far as the findings in the spinal fluid are concerned, one cannot be certain whether the red cells present were secondary to the tap or whether they actually came as the result of the cerebral lesion. If we calculate the number of white cells that would be expected with 25,000 red cells, according to the method described by Solomon, allowing 1 white cell for every 700 red cells, we obtain 300 white cells, and subtracting this from 2100, we still have some 1800 white cells to account for. Again, the protein of 198 mg. as compared with a normal of from 15 to 45 mg. is markedly increased. We can account for the amount of protein which would have been added to the spinal fluid by the presence of blood serum by allowing 1 mg. increase in the protein for every 750 red cells. This, however, gives an increase of only 33 mg., so that we still have 150 mg. to account for on another basis. The normal value of the sugar in the spinal fluid is around 60 mg., and here it is decreased by almost half. The differential count of the white cells shows a predominance of polymorphonuclears, and this along with the increased protein and the low sugar are, to me, very definite evidence of bacterial infection within the meninges. We then note that her vaginal discharge increased in amount and became foul smelling. This may indicate imperfect involution of the uterus, or even the onset of uterine infection. A red-cell count at this time showed that the patient had developed a somewhat more marked degree of anemia than was present at entrance. This might have been secondary either to her rather severe infection, to bleeding following the abortion, or to both.

An x-ray at this time showed a definite area of cavitation in the shadow at the right hilus region noted before, and at this time the neurological examination showed more definite signs localizing a lesion in the region of the left motor cortex. We then find a note that the patient was started on prontylin, I suppose because it was suspected she was suffering from a severe streptococcal infection. Apparently her chlorides had been repleted, as a second determination showed a normal value of 98 cc. of N/10 sodium chloride. The carbon-dioxide combining power, however, was definitely decreased, indicating some acidosis. This may have been secondary to her infection but it has also been described following the administration of prontylin. The neurological findings increased, with the development of an external strabismus on the right and a paralyzed right leg.

There is little doubt in my mind that this patient was suffering from some very severe infection. From the nature of her temperature chart I should strongly suspect, even though the blood cultures were negative at various times during her stay in the hospital, that she had a blood-stream infection. The only clue we have as to the nature

of the infection is that on one occasion hemolytic streptococci were cultured from the sputum. There is nothing in the story inconsistent with a severe streptococcal infection and subsequent septicemia.

Is it possible to reconstruct the events in the course of this patient's illness? If we follow what we are given, we will have to assume that her original urinary symptoms represent the onset of the illness which eventually caused her death or that the urinary infection was entirely unassociated. I believe it is perfectly possible that the infection may have begun in her kidneys. I believe she developed an extensive bronchopneumonic process probably due to the streptococcus, and it is very characteristic of these lesions to break down rapidly and cavitate. This type of pulmonary lesion is hemorrhagic in nature, similar to those that are described as having occurred during the influenza epidemic of 1918.

We still have to explain the cause and the nature of her neurologic symptoms. As mentioned above, I believe there can be no doubt this patient actually had infection in her meninges. It is possible that the blood which was found in the spinal fluid was related to the original lesion, perhaps due to thrombosis of a vessel with subsequent hemorrhage, but one cannot be sure of this. The blood was more likely due to trauma incident to performing the lumbar puncture. I believe that the patient had a definite meningitis caused by the same organism which was responsible for her pneumonia, presumably a streptococcus, and this in itself would have been enough to explain all the neurologic findings. The other possibility is that the patient, having developed abscesses in her lung, had a metastatic lesion in her brain secondary to this. This lesion would have to be located in the region of the left motor cortex, as all of her neurologic signs were on the right side. The sudden onset of these symptoms is perhaps somewhat in favor of an embolic lesion which later went on to true abscess formation, in other words, a septic embolus. If the patient had a septicemia, metastatic lesions of course might have developed anywhere. There is one other possibility which should be thought of as having produced metastatic lesions. If this patient did have a septicemia, she may also have had an acute endocarditis, perhaps even with acute vegetations containing organisms. If this was so, again, metastatic lesions could have developed anywhere. But we have no evidence that the patient did have septic endocarditis, and she certainly did not have clinical evidence of emboli elsewhere.

Although we have very little to go on, it is interesting to speculate as to whether this patient had a renal lesion of any severity. We have only one urine examination, and I have already spoken of the discrepancy in the specific gravity. If this was confirmed by subsequent examination,— that is, if the specific gravity remained consistently low, showing inability of the kidney to concentrate,—we might suspect this patient did have some degree of pyelonephritis secondary to this and the previous attack of urinary infection, both associated with pregnancy. In patients who have repeated urinary infections, we not infrequently find congenital anomalies of the urinary tract. It is possible, of course, that these may be present, but we have no evidence of them. I do not believe tuberculosis has to be seriously considered in differential diagnosis even though there are some hints in this direction in the past and family histories. The x-ray findings are not at all those of tuberculosis, and as stated above, I believe tubercle bacilli would certainly have been found if the pulmonary infection were due to this cause. We also have nothing to make us believe that this patient was suffering from miliary tuberculosis. The one other possibility is that the lesion at the right hilus might have represented tumor. If this was so, it is quite within reason that, if the lesion was located in a bronchus, secondary obstruction and subsequent abscess formation might have taken place. I do not believe that we have enough evidence to consider tumor as more than a very remote possibility. Finally, the patient may have had some uterine infection following her abortion.

I believe then that this patient was suffering from a severe streptococcal infection with a streptococcal pneumonia and secondary abscess formation, that she probably had a blood-stream infection with a metastatic lesion in her brain in the region of the left motor cortex, with secondary meningitis, and there may have been some endometritis. I believe that some degree of pyelonephritis may have been found at the postmortem examination.

Clinical Diagnoses

Lung abscess, postpneumonic.
Brain abscess.
Meningitis?
Miscarriage.

Dr. Ludwig's Diagnoses

Abortion.
Streptococcal pneumonia with abscess formation.
Streptococcal septicemia.
Cerebral abscess.
Streptococcal meningitis.
Endometritis?
Pyelonephritis?

Anatomic Diagnoses

Bronchopneumonia, with abscess formation.
Cerebral abscesses, multiple.
Meningitis.
Septic infarction of the spleen and liver.
Postpartum uterus.

Pathological Discussion

Dr. Tracy B. Mallory: The autopsy on the whole sustained Dr. Ludwig's clinical diagnoses and also showed in addition a very interesting and rare lesion which was not foreshadowed in any of the clinical signs or symptoms.

We found an abscess of the lung which was located in the apical portion of the right lower lobe. The lung for some distance around the abscess was consolidated, and both the location of the lesion and its appearance favor the assumption of secondary abscess formation in a pneumonic area rather than the commoner type of abscess which followed inhalation of septic material. There was an extensive terminal bronchopneumonia scattered throughout all the remaining lobes.

The central nervous system showed not only a meningitis but abscess formation. The rather indefinite localizing signs of abscess, however, are probably to be explained by the fact that three separate abscesses were present, one of which involved the left motor area, whereas the other two were in the posterior left parietal region and in the wall of the posterior tip of the right lateral ventricle. This last abscess had broken into the ventricle and there is very little doubt that this accident initiated the meningitis. The meningeal exudate was not in the least hemorrhagic, so that the blood which was obtained on lumbar puncture must have been due to trauma.

The genital organs showed a slightly enlarged uterus with a shaggy scar of the placental attachment measuring 2 cm. in diameter. There was no evidence of severe infection. The left ovary contained a corpus luteum of pregnancy.

We could find nothing in the kidneys to indicate a pyelonephritis, but the mucous membrane of the pelves and also that of the ureters and bladder were stained a deep red by the sulfanilamide which had been given.

From the pathological point of view the most interesting feature of the autopsy was the liver. Both on the external and the cut surfaces it showed a remarkable mottling of light brown and purple areas. The purple areas varied from the size of a single lobule up to several centimeters in diameter. Within these areas the divisions of the portal vein contained thrombi, some of which were attached to the intima, whereas others lay quite loose within the veins and had all the characteristics of emboli. Although portal thrombosis is by no means rare, clear evidence of gross embolism within the portal circulation is entirely new in my experience. Moreover, infarction of the liver, which is what the purple discoloration turned out to be due to, is also extremely uncommon because of the liver's double blood supply from both the portal vein and the hepatic artery. The usual source of portal thrombosis is infection in the gastrointestinal tract. That was not the case here, however, and it proved possible to find the source of the emboli. Two septic infarcts were present in the spleen, and a branch of the splenic vein immediately adjacent to one of these infarcts contained a thrombus. I think there can be little question that this thrombus at one time extended farther along the splenic vein and that fragments detached from it were responsible for the infarction in the liver.

From the bacteriological point of view the autopsy findings were rather equivocal. The autopsy was done twenty hours post mortem. The heart's blood, surprisingly enough, was sterile. Cultures from the lung abscess, the various brain abscesses and the spleen showed multiple organisms, including *Bacillus coli,* staphylococci, and nonhemolytic and alpha-hemolytic streptococci. No beta-hemolytic streptococci were recovered.

The New England
Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE ON PUBLICATIONS

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SUBSCRIPTION TERMS: $6.00 per year in advance, postage paid, for the United States; Canada, $7.04 per year; $8.52 per year for all foreign countries belonging to the Postal Union.

MATERIAL for early publication should be received not later than noon on Saturday.

THE JOURNAL does not hold itself responsible for statements made by any contributor

COMMUNICATIONS should be addressed to the NEW ENGLAND JOURNAL OF MEDICINE, 8 Fenway, Boston, Mass.

LAWS FOR PURE FOOD, DRUGS, AND COSMETICS

THE inadequacy of the existing Federal Food and Drugs Act is strikingly demonstrated by the fact that seizures of the toxic Elixir Sulfanilamide (Massengill) could be made only on the charge that the word "elixir" implied an alcoholic solution, whereas this product was a diethylene-glycol solution. Astonishing as it may seem, had the product been properly labeled a "solution," not an "elixir," no charge of violation of the law could have been brought against the company that had sold a product which, when used as directed, had caused many deaths.

This example should be shocking enough to arouse the medical profession to action on the pure food and drugs act now before Congress.

The United States Department of Agriculture in its recent report on "Deaths due to Elixir Sulfanilamide, Massengill" makes certain recommendations for legislation to protect the public from drugs which are dangerous because of their inherent toxicity. The recommendations are:

1. License control of new drugs to insure that they will not be generally distributed until experimental and clinical tests have shown them to be safe for use. The definition of what constitutes a new drug should include (a) substances which have not been used sufficiently as drugs to become generally recognized as safe, (b) combinations of well-known drug substances where such combinations have not become generally recognized as safe, and (c) well-known drug substances and drug combinations bearing label directions for higher dosage or more frequent dosage for longer duration of use than has become generally recognized as safe.

Exemption should be made for new drugs distributed to competent investigators for experimental work. A board of experts should be provided which will advise the Secretary of Agriculture on the safety of new drugs.

It is the department's view that no other form of control will effectively safeguard the public from the dangers of premature distribution of new drugs. To increase the penalties for violations and to require label disclosure of ingredients would be helpful, but by no means fully adequate.

In the interest of safety, society has required that physicians be licensed to practice the healing art. Pharmacists are licensed to compound and dispense drugs. Electricians, plumbers, and steam engineers pursue their respective trades under license. But there is no such control to prevent incompetent drug manufacturers from marketing any kind of lethal potion. It should be remembered that Doctor Massengill and his chemist Watkins are far better equipped from the standpoint of technical training than many other persons now engaged in the manufacture of drugs.

2. Prohibition of drugs which are dangerous to health when administered in accordance with the manufacturer's directions for use. This would provide a more appropriate basis of action than that on which proceedings were instituted against the "elixir." A number of dangerous drugs are now on the market against which not even a trivial charge of violation can be made.

3. Requirement that drug labels bear appropriate directions for use and warnings against probable misuse. Much injury results from insufficient directions and from lack of warning against overdosage, or administration to children, or use in disease conditions where the drug is dangerous, or possibility of drug addiction.

4. Prohibition of secret remedies by requiring that labels disclose fully the composition of drugs. Many foreign countries now impose this requirement. Many

drugs manufactured in the United States are exported to such countries under labels bearing such disclosure. The same drugs are sold to our citizens under labels that give no hint of their composition.

The physician, and the consumer who acts as physician to himself, both have a right to know what they administer.

The foregoing recommendations are limited to provisions which the department believes should be enacted to safeguard the public from the dangers of drugs of one type. That type includes the inherently toxic drugs, such as the "elixir," dinitrophenol and cinchophen. Many additional points should be considered if adequate protection is to be extended against even more widespread dangers to health and other abuses of public welfare arising from the inadequate control authorized by the present law over various other types of drugs.

The inclusion of these recommendations in the pure food and drugs act that is now being considered by Congress should be insisted upon by the medical profession. Moreover, to strengthen this law the profession should urge that the regulation and enforcement of this act be under the control of the Food and Drug Administration of the Department of Agriculture. Division of responsibility between the Food and Drug Administration and the Federal Trade Commission is disadvantageous, but is now being advocated by those interests that wish to weaken the act.

A letter from Dr. Henry Christian published in this issue of the *Journal* tells how physicians can meet their obligation in this matter. Unless they do so, the public may well feel that the profession's support of legislation which prohibits the sale of just such drugs as sulfanilamide, dinitrophenol and cinchophen except by prescription of a physician is based on self-interest rather than on concern for the public's well-being.

THE LICENSING OF HOSPITALS

THE report of the Special Commission to Study and Investigate Public Health Laws and Policies, authorized by the Massachusetts Legislature of 1935, and continued by the 1936 session, was made public December 2, 1936, and acted on by the Legislature in 1937.

The commission submitted the draft of a bill[1] which, if enacted, would provide for the licensing of all hospitals in Massachusetts by the Department of Public Health, except mental disease hospitals and those operated by the United States Government and the Commonwealth. The proposed bill also provides that local boards of health "shall have first certified to the Department of Public Health that the hospital applying for such license is approved as to location and equipment." The bill would confer on the department authority to make rules and regulations governing the operation of hospitals and would permit local health and police departments to visit and inspect the licensed hospital. Under existing law, maternity hospitals and obstetrical wards in general hospitals are licensed by the Department of Public Welfare; the proposed bill should provide that this function be transferred to the Department of Public Health, for otherwise complications might arise. The House passed the bill submitted with a few amendments, but it was rejected by the Senate in the last day of the session.

The advisability of an act requiring the licensing of hospitals seems reasonable, for although certain organizations publish lists of approved hospitals, there is no authority compelling observance of good administrative methods for the general or private hospitals in Massachusetts. The public should have the assurance of at least average quality of hospital service. Other institutions where medical care is provided, such as nursing homes and accommodations for the aged, should also be included in this licensing scheme.

The bill of last year was sponsored by the Massachusetts Hospital Association and approved by many physicians, and it is expected that a similar bill will be drawn and submitted to the Legislature of 1938.

The arguments in favor of the enactment of a suitable law providing for the licensing of hospitals, which appear in the report[2] of the commission, are logical and should be read by all who are interested in safeguarding the interests of the several classes of inmates of the institutions to which reference has been made.

REFERENCES

1. Report of the Special Commission to Study and Investigate Public Health Laws and Policies. P. 389. Commonwealth of Massachusetts, 1936.
2. *Ibid.*, p. 210.

OBITUARY

EDWARD AUSTIN ANDREWS

1871-1937

EDWARD AUSTIN ANDREWS was born in Wetmore, Kansas, April 7, 1871.

In 1896 he was graduated from the Harvard Medical School, and spent the following five years on the staff of the Children's Hospital before coming to Newton where he practiced his profession for over thirty-five years.

During this time he served for twenty-three years on the medical staff of the Newton Hospital, retiring one year ago because of age limit. He played a prominent part in drawing up rules for the safe handling of milk in the City of Newton. These rules were copied by other communities and later led to the general pasteurization of milk.

In addition to his medical duties, he gave generously of his time for the benefit of the city. For fourteen years, he was president of the Newton Centre Improvement Association and was influential in obtaining the Newton Centre library building, various playgrounds and the bathing facilities at Crystal Lake.

Doctor Andrews served the Newton Hospital well. The younger members of the profession will miss him because he was always ready and willing to give them advice; we older members shall miss him because of our many associations with him in one cause or another.

H. W. THAYER,
HENRY W. GODFREY,
DEWITT G. WILCOX,
Resolutions Committee
Newton Hospital Staff.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY

M. FLETCHER EADES, M.D., *Secretary*
19 Bay State Road
Boston

CASE HISTORY NO. 54. BLEEDING AT SEVENTH MONTH — CENTRALLY IMPLANTED PLACENTA PREVIA

Mrs. F. K., a thirty-seven-year-old gravida VII, was admitted to the hospital on October 3, 1937, in the seventh month of gestation, complaining of painless vaginal bleeding of two days' duration.

The family history was negative for malignancy, diabetes, pulmonary tuberculosis and chronic nephritis. The patient had never had a serious illness and had never been operated upon. Menstruation began at fourteen years of age with a twenty-eight-day cycle. Her last menstrual period began on March 7. One pregnancy resulted in a premature stillbirth; there were two early miscarriages and three normal-term pregnancies.

Within a week after the first missed period the patient began to spot daily. This slight bloody show continued off and on until admission to the hospital; there were two moderately severe hemorrhages which were treated by rest and sedatives at the patient's home and a third hemorrhage which began two days before admission.

On admission to the hospital the patient was bleeding very little. Examination showed moderate pallor of the conjunctivae, lips and finger tips. The pulse was weak, and the rate 110 per minute. The pupils reacted to light and accommodation, and all extraocular movements were normal. There was no nasal obstruction. The teeth were in good repair and oral hygiene was excellent. The thyroid was slightly enlarged. The heart was not enlarged; there were no murmurs. The lungs were clear and resonant; there were no rales. The fundus was two fingerbreadths above the umbilicus, and the fetal heart was heard in the midline. All reflexes were normal, and there were no varicosities of the extremities.

A blood count showed 2,700,000 erythrocytes and a hemoglobin of 62 per cent (Sahli). The urine was acid, with a specific gravity of 1.012 and no albumin or sugar; the microscopic examination showed squamous epithelium and detritus.

Complete rest in bed and careful observation were instituted. A slight blood loss occurred on several occasions during the next five days. On October 8 under perfect asepsis, digital and specular examinations were performed. The cervix was normal in appearance, not taken up, not patulous, and contained no polyp or erosion from which the bleeding might have come. Bimanual examination revealed a feeling of fullness between the cervix and the presenting part. A presumptive diagnosis of central placenta previa was made, and the patient was returned to bed. The following day she was given 500 cc. of citrated blood. About five minutes after the completion of the transfusion a reaction occurred characterized by dyspnea, substernal oppression and a rapid thready pulse. The administration of 1/6 gr. of morphine and 0.5 cc. of adrenalin (1:1000) afforded considerable relief, and ten minutes later her condition improved and the above symptoms gradually subsided.

It seemed unwise to delay operation, although it was appreciated that the baby, because of prema-

A series of selected case histories by members of the section will be published weekly.
Comments and questions by subscribers are solicited and will be discussed by members of the section.

turity, might not survive after delivery. Because of these factors, a low vertical cesarian section was performed on October 11. The placenta was centrally implanted, covering the entire os. A female child weighing 3 lb. was delivered and lived only a few hours. The patient's convalescence was normal.

On the seventh postpartum day a blood count showed 3,250,000 erythrocytes with a hemoglobin of 68 per cent (Sahli) and 7000 leukocytes with a normal differential. The patient was discharged on October 27, the sixteenth postpartum day, in good condition.

Comment. The delivery of this patient, when the chance of a viable child was questionable and in the absence of bleeding, is open to criticism. Had this patient been kept in bed in the hospital in the hope that no bleeding would occur until the baby's chance of survival was assured, it is quite likely that a viable baby would have been obtained. It is true that, at any minute, brisk hemorrhage might have necessitated operation. Under those circumstances, the operation would have been undertaken for the sake of the mother because of active bleeding, irrespective of the result on the child. The danger to her from a recurrent severe hemorrhage, occurring while she was in the hospital where delivery could be consummated within an hour, was negligible, and if a period of two weeks could have elapsed before another hemorrhage, the baby probably would have lived. There is a difference of opinion about performing a low cervical cesarian section in cases with placenta previa. Some feel that in placenta previa, because of the possibility of increased hemorrhage, there is a contraindication to low section. At any rate, an abdominal section for placenta previa on a patient who is bleeding and not in labor, after the point of viability of the fetus, is becoming generally accepted as the more conservative method of treatment.

MISCELLANY

DEATH OF DR. LAWRASON BROWN

In the death of Dr. Lawrason Brown at Saranac Lake, New York, on December 26, the profession has lost one of its foremost tuberculosis specialists. He had been actively connected with the Trudeau Sanatorium for nearly forty years, and was particularly prominent in the development of the Trudeau School of Tuberculosis, in which many physicians have received unexcelled instruction in the diagnosis and treatment of tuberculosis. He was a pioneer worker in intestinal tuberculosis and was among the first to adopt roentgenologic findings as a means of classifying pulmonary lesions.

He had been an associate editor of the *American Review of Tuberculosis* for many years. He was a member of the American Association of Physicians and a past-president of the American Climatological Association, the National Tuberculosis Association and the American Sanatorium Association.

CORRESPONDENCE

FOOD, DRUG AND COSMETIC CONTROL

To the Editor: Physicians in New England have an opportunity to give valuable help in securing better laws on pure food, drugs and cosmetics and their advertising. To find out why there is need for betterment read the editorial "When to Lock the Stable" in the December 9 issue of the *New England Journal of Medicine*. The Secretary of Agriculture at Washington says: "Electricians, plumbers and steam engineers pursue their respective trades under license. But there is no such control to prevent incompetent drug manufacturers from marketing any kind of lethal potion." Why?

The *Literary Digest* of December 18, 1937, answers as follows: "Thus it is amazing to note that today tens of thousands of physicians, the country over, are embattled concerning the development of novel government agencies for 'socializing' medicine — before they have moved noteworthily toward lifting a natural government function to a wise and effective plan. This 'lift' is tragically needed. Our government drug regulations and their enforcement are still on the plan of moronic farce."

How can we answer this challenge? By writing today, each of us, to our two United States Senators, to our local representative in the House of Representatives at Washington and to Senator Royal S. Copeland and Representative Clarence F. Lea, chairmen of the two committees studying needed legislation. Say in such a letter that you wish better control of food, drugs and cosmetics by a law that provides for labels stating their composition in full with warnings as to dangers in their use, that prevents distribution of drugs and cosmetics before they have been tested as to toxic action and that prevents general distribution to the lay public of drugs which, if used indiscriminately, might be dangerous, all to be enforced by the Food and Drug Administration of the United States Department of Agriculture, and that you wish restriction on all false and misleading advertising of these products by a strong law with penalties to be administered by the Food and Drug Administration so that there will be no divided responsibility.

Do this yourself and do it today. Then when your local medical society meets have it adopt resolutions expressing these ideas and send them to those already mentioned.

A medical profession that does nothing toward better laws for pure food, drugs and cosmetics is assuming responsibility for other deaths likely to occur under present laws. That people have died from using Elixir Sulfanilamide in recent months is a challenge to physicians. Remember that powerful interests in the drug and food trades fight against restrictive laws; they are well organized; so there is great need that every physician express himself to those who make our laws in Washington.

HENRY A. CHRISTIAN, M.D.

Peter Bent Brigham Hospital,
721 Huntington Avenue,
Boston, Mass.

RECENT DEATH

SMITH — CHARLES MORTON SMITH, M.D., died at his home, 437 Marlboro Street, Boston, January 8. He was in his seventy-second year.

Born in Dublin, New Hampshire, he was educated in the public schools there, attended Harvard College and was graduated from Harvard Medical School in 1893. He served an internship at the Boston City Hospital and returned to Harvard Medical School in 1895 to do postgraduate work.

Dr. Smith, one of the country's foremost authorities on syphilis, was professor emeritus of syphilology at the Harvard Medical School. An expert on genital syphilis, he served at the Boston Dispensary under Dr. Abner Post, American pioneer in syphilis research and treatment. Dr. Smith had been chief of the syphilis clinic of the Massachusetts General Hospital for fifteen years.

Among his affiliations were memberships in the American Dermatological Association, the New England Dermatological Society, the American Board of Dermatology and Syphilology, the Harvard Club of Boston, and the Roxbury Clinical Record Club, of which he was president at the time of his death. He was a fellow of the Massachusetts Medical Society and of the American Medical Association.

He leaves his widow, the former Mary L. Moulton; a son, Morton Smith, of Wellesley Hills; a daughter, Mrs. William D. Van Alstyne, of Princeton, N. J., and a sister, Mrs. F. Cora Graves, of Westboro.

REPORT OF MEETING

HARVARD MEDICAL SOCIETY

A meeting of the Harvard Medical Society was held on November 23 at the Peter Bent Brigham Hospital, Dr. James P. O'Hare presiding.

The first case was presented by Dr. Clark. The patient was a 52-year-old Jewish, married male. For over 20 years he had shown some bacteria and occasionally had shown a small amount of albumin in his urine. Eleven years before entry he had first shown pus cells in his urine and at this time the diagnosis of bilateral hydronephrosis and hydroureter was made by pyelography and cystography. There was a marked cystitis and a marked bilateral infection of the upper urinary tract. Since that time he had been followed in the Outpatient Department. The infection had persisted but had not been marked until one year before entry, when there was a severe exacerbation with urinary frequency, urgency, dysuria, costovertebral pain, chills and fever. During the last year he had been treated with mandelic acid, frequently with ureteral irrigation, and more recently with prontylin. In spite of this prolonged infection, the only significant signs of renal failure were a persistently low specific gravity and a large urinary output. There had been no enlargement of the heart, and the blood pressure had remained normal. He had had coronal ulcers and a persistent dermatitis which were attributed to the presence of chronic infection.

Dr. Quinby commented on the extreme difficulty of treating these cases. He stated that the course was invariably downhill. He also noted that loss of power of concentration of the urine was often the first indication of renal failure.

The second case was presented from the medical service by Dr. McClure. The patient was a 41-year-old female. Six years before entry she was found to have bilateral renal stones. She developed a left perinephric abscess which was drained on the surgical service. In spite of this drainage there were severe exacerbations of pain, and chills, and 4 months later a left nephrectomy had been done. Removal of the renal stone on the right was not attempted because of poor renal function. One year after this she was found to have hypertension and elevated blood urea nitrogen. Pus was found regularly in the urine. Two years before her final admission she developed angina pectoris and this had increased in severity. Her symptoms of uremia and of secondary anemia increased; she lapsed into coma and died.

The pathological findings in the two kidneys were compared by Dr. Ayer. The kidney removed in 1932 weighed 120 gm., that at autopsy 60 gm. Both showed a marked pyelonephritis. In addition, the kidney removed at autopsy showed marked vascular lesions, which were not present in the specimen removed in 1932.

Dr. Soma Weiss presented the paper of the evening. He first reviewed Bright's classification of nephritis and then called attention to the lack of emphasis which, until recent years, had been placed on the group originating as bacterial infection of the kidney. The attention of himself and of Dr. Frederick Parker, Jr., had first been called to this group by the finding that certain cases which had been diagnosed as essential hypertension could be explained as the end results of pyelonephritis. He then drew certain generalizations. Pyelitis as such probably does not exist. The infection, whether it be hematogenous, ascending or spread by way of the lymphatics, very soon becomes distributed throughout the pelvis and throughout the adjacent renal tissue so that the root of origin cannot be determined by pathological examination. Furthermore, the presence of the infection in the interstitial tissue and in the lymphatics enables kidneys which show no clinical evidence of infection still to be the seat of an active infectious or inflammatory process. These changes were illustrated by lantern slides. In a similar way he went on to show how kidneys which are the seat of chronic infection gradually become scarred and shrunken. This latter process can advance after the infection has disappeared. In addition to actual destruction of the glomeruli there frequently is considerable tubular destruction by blockage from below. Furthermore, vascular changes are superimposed. The presence and the extent of these changes seem to depend on how the patient reacted to his renal damage by an arterial hypertension. The changes in the arterioles themselves are usually of the hyperplastic arteriosclerotic type. They are also analogous to those changes found in the pulmonary arteries of cases of mitral stenosis in which there has been a severe degree of pulmonary hypertension and circulatory stasis. Thus the vascular changes are dependent upon the hypertension, but not entirely so, for inflammation in the kidney itself apparently has a direct effect upon the arterioles. This is best illustrated by cases of unilateral pyelonephritis. In these the arteriolar changes are definitely more marked in the affected kidney than in the normal kidney. Areas in the same kidney where the inflammation is more pronounced also show less arteriolar change than less inflamed areas in the same kidney. Just as in essential hypertension, the so-called benign and malignant types of arteriolar change are found. Their presence apparently depends on the height and rate of progression of the hypertension. Pyelonephritis is responsible for about 15 or 20 per cent of the instances of the malignant phase of hypertension. Dr. Weiss called attention to the frequency of pyelonephritis and pointed out the importance of an understanding of this condition in the fields of surgery, pediatrics, obstetrics and internal medicine. Because of the close rela-

tion of pyelonephritis to arterial hypertension of renal origin and to the small contracted kidney, pyelonephritis should be considered as one type of Bright's disease. The close interrelation between the various types of Bright's disease was emphasized.

Dr. Christian in discussing the paper made a plea for a more simplified classification of Bright's disease. He advocated a division into (1) acute stage; (2) subacute or chronic stages with edema; and (3) a chronic stage without edema. This last stage, as characterized by small shrunken kidneys, can be reached either by essential hypertension with vascular change, by glomerular damage, by infection, or even by primary tubular damage as in nephrosis.

NOTICES

REMOVAL

DAVID KUNIAN, M.D., announces the removal of his office to 19 Nahant Street, Lynn.

CAMBRIDGE HOSPITAL

The regular monthly meeting of the staff of the Cambridge Hospital will be held in conjunction with the Middlesex South District Medical Society in the lecture hall of the nurses' home at 10:00 a. m., January 19.

A clinicopathological discussion will be held. A buffet luncheon will be served at 1:00 p. m.

Please notify the director if you plan to attend.

JOSEPH M. WADDEN, M.D., *Secretary.*

TUMOR CLINIC, BOSTON DISPENSARY

Each Tuesday and Friday morning from ten to twelve-thirty there is a meeting of the Tumor Clinic of the Boston Dispensary, a unit of the New England Medical Center. All kinds of tumors are seen, discussed, and when indicated, treated with radium and high-voltage x-ray.

Physicians are welcome to visit this clinic and to bring a patient to the clinic for diagnosis.

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held in the Peter Bent Brigham Hospital amphitheater (Shattuck Street entrance), Tuesday, January 25, at 8:15 p. m.

PROGRAM

Presentation of cases.

Medical Investigations in Peru in 1937. Drs. Richard P. Strong, Henry Pinkerton, and David Weinman.

Medical students and physicians are cordially invited to attend.

MARSHALL N. FULTON, M.D., *Secretary.*

JOINT MEETING OF THE SUFFOLK DISTRICT MEDICAL SOCIETY AND THE BOSTON MEDICAL LIBRARY

There will be a joint meeting of the Suffolk District Medical Society and the Boston Medical Library at the Boston Medical Library, 8 Fenway, on Wednesday, January 19, at 8:15 p. m.

The "Principles and Proposals" will be discussed by the following: Dr. Robert B. Osgood, Dr. Frank H. Lahey, Dr. Channing Frothingham, Dr. Elliott P. Joslin, Dr. Richard M. Smith and Dr. Roger I. Lee.

JOHN P. MONKS, M.D., *Secretary,*
Suffolk District Medical Society.

JAMES M. FAULKNER, M.D., *Secretary,*
Boston Medical Library.

CARNEY HOSPITAL

The monthly clinical meeting and luncheon of the Carney Hospital Staff will be held on Monday, January 17, in the Andrew Carney Assembly Hall, at 11:30 a. m.

PROGRAM

Case reports:

Epidural Cyst with Removal and Recovery.

Polycythemia.

Carcinoma of Cervix Treated with Radium: Subsequent Removal of Rapidly Growing Ovarian Tumors.

Pathological exhibit.

Determination of Blood Loss in Certain Standard Operations for Malignancy. Dr. Weston Buddington. Discussion by Drs. A. Fraser, William C. Moloney and Roy J. Heffernan.

Physicians and students are cordially invited to attend.

ROY J. HEFFERNAN, M.D., *Secretary.*

"GREEN LIGHTS TO HEALTH"

The following change in the "Green Lights to Health" broadcast, being given over Station WAAB at 7:30 p. m., on Wednesdays, has been announced. Dr. Elliott S. Robinson will speak on January 19. His subject will be "The Laboratory Fights Pneumonia."

BOSTON MEDICAL HISTORY CLUB

There will be a meeting of the Boston Medical History Club at the Boston Medical Library, 8 Fenway, on Monday, January 17, at 8:15 p. m.

Dr. Donald S. King will talk on "The Development of Our Knowledge of the Lung and Its Diseases."

BENJAMIN SPECTOR, M.D., *Secretary.*

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular meeting of the New England Society of Physical Medicine will be held at the Hotel Kenmore, on Wednesday evening, January 19, at 8:00.

PROGRAM

Some Fundamental Types of Physical Medicine and Their Practical Application. Dr. Franklin P. Lowry. Demonstrated by Miss Esther Klein. Discussion — Dr. Howard Moore.

The council will meet at 6:00; dinner will be served in the Empire Room at 6:30.

All members of the medical profession are cordially invited to attend.

WILLIAM D. MCFEE, M.D., *Secretary.*

THE NORFOLK DISTRICT MEDICAL SOCIETY

The regular meeting of the Norfolk District Medical Society will be held in the Hotel Kenmore, on January 25, at 8:15 p. m. Tel. Ken. 2770.

Business:

Report of Committee Investigating Minimum Fees to Be Charged for Services to Welfare Recipients. It is hoped that all interested in this work will attend.

Incidental business.

Communication:

The Management of Uterine Prolapse. Dr. Louis E. Phaneuf.

Collation.

FRANK S. CRUICKSHANK, M.D., *Secretary.*

NEW ENGLAND HEART ASSOCIATION

The next meeting of the New England Heart Association will be held at the Peter Bent Brigham Hospital, on Monday, January 24, at 8:15 p. m.

PROGRAM

The Development of Fatal Luetic Aortitis within Two Years After Primary Infection. Dr. Maurice A. Schnitker.

Errors in the Direct Method of Measuring Venous Pressure. Dr. Richard H. Lyons.

Physiological Effects of Artificial Fever. Dr. John A. Gibson, 2nd.

The Incompatibility of Hypertension and Active Tuberculosis. Dr. A. W. Contratto.

The Prognosis of Potential Rheumatic Heart Disease and Rheumatic Mitral Insufficiency. Drs. John A. Boone and Samuel A. Levine.

The Precordial Lead. Drs. Roger S. Robinson and A. W. Contratto.

Interested physicians and medical students are invited to attend.

JAMES M. FAULKNER, M.D., *Secretary.*

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

The next meeting of the Boston Society of Psychiatry and Neurology will be held at the Boston Medical Library, on Thursday evening, January 20, at 8:15.

PROGRAM

Annual election of officers. Reports of secretary and treasurer.

Human Credulity as Illustrated by Witchcraft. Dr. Theodore Diller, of Pittsburgh, Pennsylvania.

H. HOUSTON MERRITT, M.D., *Secretary.*

BOSTON SOCIETY OF ANESTHETISTS

The next meeting of the Boston Society of Anesthetists will be held on Tuesday, January 25, at the Hotel Kenmore.

PROGRAM

Dinner. 6:30 p. m.

Business meeting. Election of officers. 7:40 p. m.

Scientific meeting. 8:15 p. m. Dr. Soma Weiss will speak on "Preanesthetic and Postanesthetic Problems from the Point of View of the Internist."

Physicians and medical students are cordially invited to attend.

ELEANOR B. FERGUSON, M.D., *Secretary.*

THE MASSACHUSETTS SOCIETY FOR SOCIAL HYGIENE

The Massachusetts Society for Social Hygiene is sponsoring an open meeting at Ford Hall, 15 Ashburton Place, Boston, Thursday evening, January 20, at 8:15.

Dr. Stanley H. Osborn, commissioner of health of the State of Connecticut, will speak on "The Connecticut Blood-Test-Before-Marriage Law," and will describe its genesis, its provisions and the way in which it has so far worked out.

Dr. Nels A. Nelson, director of the Division of Genito-infectious Diseases of the Massachusetts Department of Public Health, will discuss Dr. Osborn's paper. Dr. Nelson is opposed to such legislation and the meeting will thus give an opportunity for those who attend to hear both sides of this important question. There will be opportunity also for open discussion from the floor.

This meeting will be of particular interest to physicians, legislators, social workers and other professional workers. The meeting is open to the public and a cordial invitation is extended to all who are interested. There will be no admission fee.

TUFTS MEDICAL ALUMNI CLUB OF WORCESTER COUNTY

There will be a meeting of the Tufts Medical Alumni Club of Worcester County at the Bancroft Hotel, Worcester, on Wednesday, January 19. Dinner at 6:30 p. m. will be followed by a business meeting at 7:30 p. m.

Dr. Henry W. Hudson, Jr., will speak on "Conceptions and Misconceptions of Surgery in Infancy and Childhood."

C. BYRNE, M.D., *President,*
N. S. SCARCELLO, M.D., *Secretary.*

LECTURES AT THE FAULKNER HOSPITAL

A series of illustrated, public, health lectures at the Faulkner Hospital will be held in the hospital auditorium at 4 p. m. on Sundays. The schedule is as follows:

January 16 — Heart Ailments and Their Prevention. Dr. Burton E. Hamilton.

January 23 — Common Colds and Their Prevention. Dr. James A. Halsted.

January 30 — Skin Evidences of General Ill-Health. Dr. E. Lawrence Oliver.

February 6 — Practical Hints for the Expectant Mother (women only). Dr. D. J. Bristol, Jr.

February 13 — Stomach and Duodenal Ulcer. Dr. Edward S. Emery, Jr.

February 20 — Progress in Dental Surgery. Dr. Kurt H. Thoma.

February 27 — Backache. Dr. John D. Adams.

March 6 — Chest Operations in the Treatment of Tuberculosis. Dr. Harlan F. Newton.

March 13 — Diets and Vitamins in the Preservation of Health. Dr. Maurice B. Strauss.

March 20 — Diseases of the Prostate Gland (men only). Dr. Franklin Balch, Jr.

March 27 — Hay Fever and Asthma. Dr. Walter S. Burrage.

April 3 — "Nerves" and Their Relation to Insanity. Dr. Merrill Moore.

April 10 — Common Foot Ailments and Their Significance. Dr. Lloyd T. Brown.

April 24 — Syphilis: Its cause, prevalence and eradication. Dr. Channing Frothingham.

NEW ENGLAND PATHOLOGICAL SOCIETY

There will be a meeting of the New England Pathological Society in the large amphitheater of the Children's Hospital on Thursday, January 20, at 8:00 p. m.

Dr. C. P. Rhoads, Rockefeller Hospital, New York, will speak on "The Pathologic Morphology and Physiology of Refractory Anemia."

Physicians and medical students are cordially invited to attend.

J. B. HAZARD, M.D., *Secretary*.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, JANUARY 17

MONDAY, JANUARY 17

*11:30 a. m. Carney Hospital, clinical meeting. Andrew Carney Assembly Hall.

8:15 p. m. Boston Medical History Club. Boston Medical Library, 8 Fenway.

TUESDAY, JANUARY 18

*9-10 a. m. Boston Dispensary. Types of Hemolytic Anemia. Dr. William Dameshek.

*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

*12 m. South End Medical Club. Headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston.

WEDNESDAY, JANUARY 19

*9-10 a. m. Boston Dispensary. Clinicopathological conference. Dr. R. C. Wadsworth, Dr. Robert W. Buck.

*12 m. Clinicopathological conference. Children's Hospital Amphitheater.

*8 p. m. New England Society of Physical Medicine. Hotel Kenmore, Boston.

THURSDAY, JANUARY 20

8:30-9:30 a. m. Exchange visit, surgical and orthopedic staffs of the Peter Bent Brigham and Children's hospitals, held this week at the Children's Hospital.

*9-10 a. m. Boston Dispensary. Recent Advances in the Treatment of Pulmonary Tuberculosis. Dr. M. H. Holden.

*8 p. m. New England Pathological Society. Amphitheater of Children's Hospital.

8:15 p. m. Boston Society of Psychiatry and Neurology. Boston Medical Library, 8 Fenway.

8:15 p. m. Massachusetts Society for Social Hygiene. Ford Hall, 15 Ashburton Place, Boston.

FRIDAY, JANUARY 21

*9-10 a. m. Boston Dispensary. Here and There in Endocrinology. Dr. Fuller Albright.

*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

12 m. Clinical meeting of the Children's Medical Service, Massachusetts General Hospital, Ether Dome.

SATURDAY, JANUARY 22

*9-10 a. m. Boston Dispensary. Hospital Case Presentation. Dr. Samuel H. Proger.

*10 a. m. - 12 m. Staff rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Henry A. Christian.

SUNDAY, JANUARY 23

4 p. m. Free public lecture. Harvard Medical School, amphitheater of Building D. Teeth: Deciduous, Permanent and Artificial. Dr. Paul E. Boyle.

4 p. m. Free public lecture. Beth Israel Hospital, Boston, in conjunction with the Women's Auxiliary. What to Do About Cancer. Dr. Harry F. Friedman.

4 p. m. Illustrated, public, health lecture. Faulkner Hospital. Common Colds and Their Prevention. Dr. James A. Halsted.

*Open to the medical profession.

JANUARY 14 — Tumor Clinic, Boston Dispensary. Page 94.

JANUARY 16 - APRIL 24 — Illustrated, public, health lectures. Faulkner Hospital. Page 95.

JANUARY 17 — Carney Hospital. Clinical meeting. Page 94.

JANUARY 17 — Boston Medical History Club. Page 94.

JANUARY 18 — South End Medical Club. Page 51, issue of January 6.

JANUARY 19 — Tufts Medical Alumni Club of Worcester County. Page 95.

JANUARY 19 — Cambridge Hospital, regular monthly staff meeting. Page 94.

JANUARY 19 — New England Society of Physical Medicine. Page 94.

JANUARY 20 — Boston Society of Psychiatry and Neurology. Page 95.

JANUARY 20 — Massachusetts Society for Social Hygiene. Page 95.

JANUARY 20 — New England Pathological Society. Notice above.

JANUARY 24 — New England Heart Association. Page 95.

JANUARY 25 — Harvard Medical Society. Page 94.

JANUARY 25 — Boston Society of Anesthetists. Page 95.

FEBRUARY 1 — Greater Boston Medical Society. Auditorium of the Beth Israel Hospital, Boston, 8:30 p. m.

FEBRUARY 2 — Second National Social Hygiene Day. Page 49, issue of January 6.

FEBRUARY 10 — Pentucket Association of Physicians. Hotel Bartlett, 95 Main Street, Haverhill, 8:30 p. m.

FEBRUARY 14 — American Board of Internal Medicine. Page 969, issue of December 9.

MARCH 10, 11, 12 — New England Hospital Association. Page 51, issue of January 6.

APRIL 4-8 — The American College of Physicians. Page 41, issue of July 1.

MAY 31, JUNE 1 and 2 — Annual meeting of the Massachusetts Medical Society. Hotel Bradford, Boston.

OCTOBER 17-21 — Clinical Congress of the American College of Surgeons, New York City.

DISTRICT MEDICAL SOCIETIES

BRISTOL SOUTH

MAY 5 — 5 p. m., New Bedford.

ESSEX SOUTH

FEBRUARY 2 — Council Meeting, Boston.

FEBRUARY 9 — Essex Sanatorium, Middleton. Clinic at 5 p. m. Dinner at 7 p. m. Speaker: Dr. John B. Hawes, 2d. Subject: Dust and Disease.

MARCH 2 — Lynn Hospital. Clinic at 5 p. m. Dinner at 7 p. m. Speaker and subject to be announced.

APRIL 6 — Gloucester Hospital, Gloucester. Clinic at 5 p. m. Dinner at 7 p. m. Speaker and subject to be announced.

MAY 5 — Censors meet at Salem Hospital, 3:30 p. m.

MAY 11 — Annual meeting, Salem Country Club, Peabody. Dinner at 7 p. m. Speaker and subject to be announced.

FRANKLIN

Meetings will be held at the Franklin County Hospital, Greenfield, at 11 a. m. the second Tuesdays of March and May.

HAMPDEN

Meetings will be held on the fourth Tuesday in January, April and July.

MIDDLESEX EAST

Meetings will be held at the Bear Hill Golf Club, Stoneham, at 12:15 p. m. on March 16, and May 11.

MIDDLESEX NORTH

Meetings will be held at the Vesper Country Club, Lowell, on January 26 and April 27.

MIDDLESEX SOUTH

JANUARY 19 — Page 1113, issue of December 30.

NORFOLK DISTRICT

JANUARY 25 — Page 94.

FEBRUARY 23 — Hotel Kenmore. 8:15 p. m. Dermatitis Venenata Due to Cosmetics and Industrial Irritants. Dr. John G. Downing. Discussion by Dr. Francis P. McCarthy.

MARCH 29 — Hotel Kenmore. 8:15 p. m. Subject to be announced but to be related to diseases of the kidney. Dr. Albert A. Hornor.

MAY — Annual meeting.

The censors meet on the first Thursdays of May and November in each year.

NORFOLK SOUTH

Meetings held at 12 noon.

FEBRUARY 3 — Norfolk County Hospital, South Braintree.

MARCH 3 — Norfolk County Hospital, South Braintree.

APRIL 7 — At the Quincy City Hospital.

MAY 5 — Annual Meeting.

PLYMOUTH

Meetings will be held at 11 a. m. on January 20, March 17, April 21, May 19 and July 21.

SUFFOLK

JANUARY 19 — Joint meeting with Boston Medical Library. Page 94.

MARCH 15 — Joint meeting with Boston Obstetrical Society.

WORCESTER

At the following meetings, except the annual meeting, dinner will be at 6:15, to be followed by business session and scientific program.

FEBRUARY 9 — Worcester State Hospital, Worcester.

MARCH 9 — Memorial Hospital, Worcester.

APRIL 13 — Hahnemann Hospital, Worcester.

MAY 11 — Afternoon and evening, annual meeting. Place and schedule of program to be announced.